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Original Communications

OBSERVATIONS ON BLOOD SUGAR AND SERUM CALCIUM IN RELATION TO LACTATION IN WOMEN, WITH A STUDY OF ITS POSSIBLE RELATIONSHIP TO PARTURIENT PARESIS

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GENERAL INTRODUCTION

AMONG the many theories that have been brought forward to explain the etiology of "eclampsia" there has been one of mammary origin. Certain clinical similarities (convulsions, coma, albuminuria) between "milk fever," or parturient paresis, in cattle, and the toxemias of later pregnancy in women, similarities extending even to method of treatment up to 1897 (purgation, venesection, hot packs) led to a comparison of the two conditions. The discovery in 1897 by Schmidt,[1] that so simple a procedure as the injection of a small amount of potassium iodide solution into the udder (a process afterward improved by its inflation by air by Anderson[2]), led to a reduction in the mortality of "milk fever" in cattle from 40 to 50 per cent down to 1 to 2 per cent, could not fail to have a repercussion in human obstetrics at a time when the mortality from "eclampsia" was still distressingly high. Thus, despite dissimilarities (relation of occurrence to parturition, relation of incidence to parity) there were not found wanting obstetricians who applied the procedure of mammary insufflation, and even mammary ablation to "eclampsia" in women, unfortunately without the almost uniformly happy result attained by their brethren in veterinary practice. Wilson[3] in 1913 gave an excellent

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summary of those procedures up to that time. Since then theories of the mammary origin of "eclampsia" have fallen into disuse, though there are not wanting investigators who still believe that the theory may prove of assistance. Thus Kosmak[4] believes the subject may still prove worthy of study. Greig and Browne[5] have been experimenting on simple and efficient means of inflating the human breast. Our own reason for reviving the comparison is that recently there has occurred a recrudescence of experimental work on the condition in cattle, a review which, together with a study of the possibility of analogous conditions in women, may prove of interest to both branches of practice. Recent theories which have been proposed on the origin of parturient paresis in cattle are (a) disturbance in carbohydrate balance as exemplified by blood-sugar estimations, (b) guanidine intoxication consequent on parathyroid deficiency, (c) disturbance in level of blood calcium. It would be natural to connect the two latter theories, though they were proposed separately by their respective authors. At the onset it should be understood that "milk fever" in cattle is not per se attended by rise in temperature. A subnormal temperature characterizes the condition. In many cases a raised temperature is observed, but this is generally ascribed to a concurrent infection. Also it is the general well-confirmed observation that "milk fever" is a disease attacking heavy-milking cows. It is usual to ascribe the success of the therapeutic mammary insufflation to the suppression of milk flow.

BLOOD SUGAR IN LACTATION IN COWS

The experiments of Porcher, Foa, Kaufman and Magne, and Cary as reviewed by Meigs[6] form strong evidence that the lactose of milk is formed from the glucose of the blood. A review of the level of blood sugar in lactating as compared with nonlactating cows shows a much lowered level in the former. In Table I, we have collected some of the results in the literature bearing on this point. The difference between the two states in the same species is marked except in man, and it is a reasonable assumption that the lowered blood glucose observed in the lactating animal is due to the demand on that sugar for the formation of lactose. Widmark and Carlens have calculated that a cow giving 28 kg. milk per day is under the strain of regenerating the whole of its circulating blood glucose every fifteen minutes. They have also endeavored to show that the level of the blood sugar is inversely as the intensity of the lactation. Table II, copied from their own paper,[7] is given as evidence of this assertion. In this connection too we may draw attention to the observation of Markowitz and Simpson[14] on the hypoglycemia observed in a totally depancreatized dog twenty-four hours after parturition. The amount of insulin which was sufficient to maintain a normal circulating glu-

TABLE I. SHOWING THE EFFECT OF LACTATION ON BLOOD SUGAR IN COWS, ETC.

SUBJECT	OBSERVERS	GLUCOSE, MG. PER 100 C.C. BLOOD, MG.
Cow (Dry)	Widmark and Carlens[7]	Av. 80
Cow (Lactating)	Widmark and Carlens	Av. 60
Cow (Dry)	Auger[8]	90–120
Cow (Lactating)	Auger	55– 75
Cow (Lactating)	Hayden and Sholl[9]	Av. 52
Goat (Dry)	Auger[8]	70–100
Goat (Lactating)	Auger	55– 65
Man (Normal)		80–120
Woman (Pregnancy)		80–120
Woman (Postpartum 7 days)	Bergsma[10]	Av. 94
Woman (Postpartum 7 days)	Morriss[11]	Av. 109
Woman (Postpartum 2 days)	Rowley[12]	Av. 140
Woman (End of labor)	Caldwell and Lyle[13]	Av. 95

TABLE II. SHOWING THE RELATION OF BLOOD SUGAR TO MILK YIELD IN DAIRY COWS ACCORDING TO WIDMARK AND CARLENS

COW	DAILY MILK OUTPUT KG.	AVERAGE BLOOD SUGAR PER CENT
A	18	0.053
B	14	0.057
C	10	0.057
D	8	0.058
E	6	0.061
F	0	0.076
G	0	0.081

cose in pregnancy was insufficient during lactation. If these are the facts connecting the output of milk and the level of the blood sugar it requires very little effort to imagine circumstances in which a high milk-producing cow might lower the blood sugar to such an extent that the clinical manifestations of hypoglycemia would make their appearance. Such is the theory of etiology of parturient paresis as proposed by Auger[8] in France. Widmark and Carlens[15] in Denmark and Maguire[16] in England have independently proposed theories of hypoglycemia as the origin of "milk fever." All three have shown the occurrence of blood sugar lowered to symptomatic levels in "milk fever" in support of their claims and have claimed the rapid cure of the clinical condition by the injection of glucose solutions. Widmark and Carlens, and Auger have produced hypoglycemia in lactating cattle by insulin, and noted its similarity to parturient paresis. Although we have given in logical sequence a series of steps by which it might be assumed that hypoglycemia was the cause of "milk fever" in cattle, actually the possibility of a relationship between the two was pointed out from the similarity of the clinical symptoms in cows, and those of insulin hypoglycemia in rabbits, by an unknown Canadian veterinarian, who employed intravenous glucose solutions for its relief. This was reported by Neefs.[17]

The origin of parturient paresis in cattle which we have just presented has not escaped challenge. Little and Keith,[18] Hayden,[19] and Fish[20] have all failed to observe hypoglycemia in this condition. The findings of Hayden and Sholl, and Hayden, in particular, point to a hyperglycemia. Nevertheless the theory of hypoglycemia as the etiologic factor in milk fever is a powerful influence in veterinary practice.

Is there any analogue to be found in human obstetric practice? In this connection it is of interest to note the recent publication of Titus[21] claiming the presence of a relative hypoglycemia in "eclampsia" in women, to which the convulsive attacks should be ascribed, and reemphasizing his views on the value of intravenous glucose solutions in this condition. It is more usual to view "eclampsia" as accompanied by hyperglycemia. As far as lactation is concerned the level of blood sugar in women is usually regarded as similar to the pregnant or nonpregnant; i.e., 80-120 mg. (Table I). Such figures, however, do not take into account the probability of a decreased blood sugar due to excessive lactation similar to that claimed as occurring in cows by Widmark and Carlens. We have carried out a series of observations to this end, correlating the level of the blood sugar and the milk production.

THE TWO HOUR LACTATION TEST

In order to estimate the milk production of a series of women we devised a procedure which we have called the "two hour lactation test." The breasts are exhausted at 7 A.M. by an electric breast pump and again at 9 A.M. No food or water is given during this period, and the patient has fasted from the previous evening's meal. The amount of milk collected from 7 A.M. to 9 A.M. is taken as the "two hour lactation test" for the day. This is repeated on two successive mornings, and the average of the three measurements is taken as an index of the milk producing capacity of the subject. The test shows daily fluctuations but these are not usually large. Table III shows the ordinary fluctuations encountered in a number of cases. Repeated tests on three or four cases showed a similar average. Occasionally a case was encountered where the fluctuations greatly exceeded the general average fluctuation. This was encountered in women whose knowledge of English was insufficient to enable them to understand the procedure about to be carried out, and who were apprehensive of its effect. This usually disappeared on the second or third morning of the test. Occasionally, also, the effect of some external disturbance, usually of a family nature, the news of which was brought into the hospital by a visitor, made itself evident on the milk output. These emotional fluctuations were discounted in the final average. Examples of these are shown in Table III. All tests were carried out on the tenth, eleventh and twelfth day postpartum. All

TABLE III. ILLUSTRATING "TWO-HOUR LACTATION TEST"

SUBJECT	GRAVIDA	AGE	HEIGHT FT.—IN.	WEIGHT LB.	MILK OUTPUT				
					1	2	3	AVERAGE	AVERAGE PER SQ. METER
					c.c.	c.c.	c.c.	c.c.	c.c.
P–n	ii	18	5— 4	142½	55	55	55	55	32.7
M–n	ii	30	5— 4¾	143¼	75	50	40	55	32.5
M–n	ii	18	4—11	95	20	40	10	23	12.5
S–e	i	19	5— 2	108¾	20	10	15	15	10.1
P–r	iii	27	5— 3½	115¾	20	25	20	21	14.1
C–m	i	22	4— 9½	106¼	40	45	35	40	28.9
P–r	i	27	5— 2¾	102½	45	30	50	41	28.6
B–g	i	24	4— 8¾	118¾	40	50	80	56	39.3
K–y	iii	26	5— 3	109	30	30	25	28	19.1
W–s	v	24	5— 4	122½	15	15	0*	15	9.9
S–l	ii	21	5— 3	165	30	25	45	33	18.8
P–g	i	24	5— 4½	127¾	25	25	30	26	16.5
M–n	iv	33	5— 2½	120	55	75	50	60	38.9
B–m	iii	25	5— 3	128	45	40	65	50	31.4
Mc–y	iii	30	4—11½	105½	75	70	62	69	48.2
S–y	i	18	5— 1½	110	5	7	10	7	5.0
P–s	i	30	5— 2	127	5	7	20	10	6.7
P–s†	i	30	5— 2	127	15	15	15	15	9.5
D–f	i	23	4—11¼	101¼	10*	3*	50		
S–l	ii	21	5— 3	111	50	10*	50	50	33.3

*Emotional Fluctuation.
†Repeat 10 days later.

cases were normal, developing no complications during the puerperium and receiving the same general diet. This ensured as equal conditions for the test as we think could be secured in a general maternity hospital. All tests were carried out under the supervision of one graduate nurse.

In order to equalize the possible effect of differences in weight, etc., on the milk-producing capacity of the subject, the average results of the two hour lactation test were corrected to the unitary standard of one square meter of surface area. The surface area was calculated from the heights and weights of the subject taken on the last morning of the test (Table III) using the Aub-Dubois table.

In Fig. 1 is shown the percentage occurrence of women according to their milk producing power as shown by the two hour test per sq. meter, with the milk producing power given in units of 10 c.c. The general average secretion of milk varies from 10 to 40 c.c.; 130 subjects were examined and 93, or 71.5 per cent, lie between these figures; 17 subjects, or 13.1 per cent, secreted below 10 c.c. A small group of 20, or 15.4 per cent, would evidently be considered as high milk producing women, giving over 40 c.c. of milk per square meter surface per two hours. According to our test the women would thus divide themselves into three groups of low, average, and high milk producers. The rather wide range of milk secretion of the average group is a result probably of the effect of various physical factors in the individual women. The large number in this group gives us confidence in

our average analytical findings in the blood specimens. On the other hand it diminishes to a rather small figure the number of women in the low and high lactating groups.

It is pertinent to inquire, however, whether the two hour lactation test is an accurate or even an approximate reflex of the lactating powers of the subject. Were the mammary gland a machine, and working with machine-like exactitude, we might expect the two hour test to represent one-twelfth of the twenty-four hour milk production. In general, this seems to be so, for the average value of the ratio of the two hour test to the twenty-four hour output (ratio $\frac{b}{a}$) is 11.55 (Table IV) for the 60 cases studied. Individually, other factors,

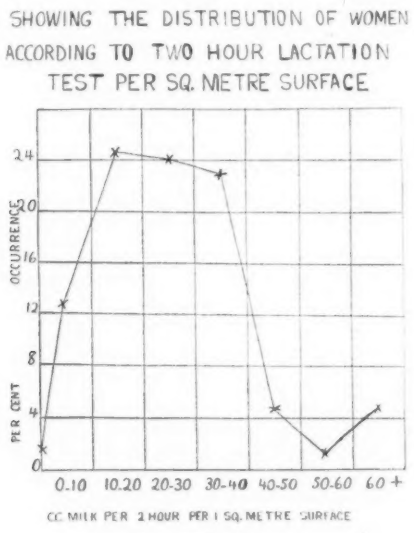

Fig. 1.

particularly those of emotion, etc., easily destroy this relationship. The ratio $\frac{b}{a}$, however, is not constant for the different groups of lactating women. In general, however, the woman who shows a low two hour lactation test shows a low twenty-four hour output. The average two hour test corresponds to an average daily output, etc. This is shown in Table IV, arranging the observations according to the two hour test in units of 10 c.c. (The figures in this table are shown as actually obtained and not reduced to 1 sq. meter surface.) The striking feature of these observations is the gradually decreasing value of the ratio $\frac{b}{a}$. The twenty-four hour output was determined on the tenth day postpartum commencing with the two hour test, weighing the baby before and after each nursing, and then measuring the milk exhausted from the breasts at 7 A.M. of the eleventh day

postpartum. In this way the full twenty-four hour output from 7 A.M. on the tenth day to 7 A.M. on the eleventh day postpartum was obtained. Such a determination involving a number of separate weighings on hospital scales should be susceptible to a greater number of errors than the two hour test. The regularity of the ratio $\frac{b}{a}$ as shown in Table IV, however, convinces us that both sets of observations are substantially correct. What is the explanation of the decreasing ratio $\frac{b}{a}$ with the increasing two hour lactation? How regular this decrease is may be seen if the ratio $\frac{b}{a}$ is plotted against the two hour lactation test as shown in Fig. 2. The smoothed curve as drawn is so

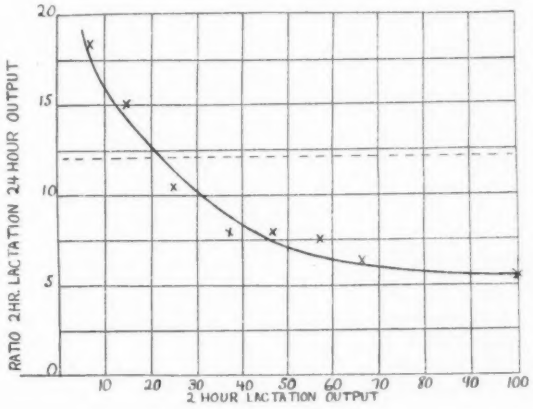

Fig. 2.

regular that one cannot help but suspect some biologic relation. A hint of what perhaps this may be is given if we suppose that the low lactating woman is under a greater stimulus to milk production than the high lactating woman. The two hour lactation test represents what should be a constant stimulus to all classes of lactating women.

TABLE IV. RELATIONSHIP OF TWO HOUR LACTATION TEST AND TWENTY-FOUR HOUR OUTPUT OF MILK

a AVERAGE 2 HR. TEST	b 24 HR. OUTPUT	NO. OF OBSERVATIONS	RATIO $\frac{b}{a}$
c.c.	c.c.		
7.3	137	1	18.7
15.2	225	9	15.1
24.2	281	10	11.7
34.1	301	8	8.8
42.7	353	13	8.2
53.4	416	11	7.7
65.1	447	5	6.8
118.2	657	3	5.4
Average ratio $\frac{b}{a}$ for total of 60 cases			11.55

It represents the ability of the gland to produce milk after the breasts have once been emptied. This, however, represents what is happening daily to the low milk producing woman. The suckling of the baby exhausts, or nearly exhausts, the breasts at each nursing. The glands are thus periodically stimulated to their maximum, or nearly so, several times during the twenty-four hours. With the high lactating woman, this is not so. The baby by no means exhausts the breasts at each feeding, leaving some milk in the gland to act as an inhibitory factor to its activity.* The twenty-four hour milk output of the high lactating woman thus by no means represents the maximum capacity of glands. The two hour test gives a much better index. Even this is probably low, on account of the inhibitory effect we have just mentioned. Luckily our results of the blood analyses of these women are such that it is unlikely any error is introduced by this factor. If the explanation we have given of the variation in the ratio $\frac{b}{a}$ is correct it forms another example of the beautiful adaptation existing between the milk supply of the maternal organism and the need of the young. The low lactating mother, stimulated by the periodic emptying of her breasts by the nursing infant, maintains a relatively high output while the high lactating mother, stimulated to a lesser degree by the partial exhaustion of her glands, reduces her output. It is of interest to observe that this regulation is already in operation by the tenth day postpartum.

BLOOD SUGAR AND LACTATION IN WOMEN

Arranging our cases in this way into three classes of lactation we have determined the average blood-sugar value of each group as shown in Table V. The blood specimen for analysis was taken fasting the morning of the tenth day postpartum. The plasma was separated immediately, oxalate being used as an anticoagulant. Sugar was determined by the method of Shaffer-Hartman.[22] A specimen taken on the eleventh or twelfth morning agreed with that taken on the tenth morning. The blood-sugar values of 95, 95, and 93 mg. for the three lactation classes scarcely show any variation, especially when the small number of cases examined in the low and high groups is considered. The average value of 94 for all cases agrees with the average figures of Bergsma (90 mg.) and Caldwell and Lyle (95 mg.), and is slightly lower than that of Killian and Sherwin (111 mg.). It is, however, much lower than that of Rowley; indeed Rowley's average figure of 140 mg. is distinctly high. The range of our blood sugars, 56 to 146 mg., represents a wide range but 85 per cent of our figures fall in the usually accepted range of 80 to 120 mg. There appears little evi-

*Incomplete stripping in the milking of dairy cows is well known to lessen the yield.

TABLE V. CONNECTING THE AVERAGE BLOOD SUGAR LEVEL WITH THE LEVEL OF LACTATION

LACTATION GROUP	NO. OF CASES	BLOOD SUGAR AVERAGE 100 C.C. PLASMA	BLOOD SUGAR RANGE. 100 C.C. PLASMA	BLOOD SUGAR TOTAL AVERAGE
		mg.	mg.	mg.
*Low	16	95	72–138	
Average	93	95	62–146	95
High	21	93	57–122	

*Variations in the number of cases occurring in a particular lactation group will be noticed. This is due to the fact that more than 130 subjects were examined, but it was not possible to obtain full data in each case.

dence, then, from our figures that lactation in women is attended by any carbohydrate or endocrine disturbance, such as is shown, in cows or goats, by the average low blood sugar. Tables VI and VII further emphasize this point. In Table VI we have collected together 8 cases whose blood sugar was 75 mg. or less. The range of these cases, 56 to 75 mg. blood sugar, is distinctly below the usual range. The lactation tests show, however, that only one out of the 8 would be classed as a high lactating woman, whereas 3 would be put in a subnormal class from the point of view of milk production. In Table VII we show the 5 highest lactating women of our series. The blood sugars of all lie well within the normal range. It is interesting to note, however, that were we to rely exclusively on the data of Table VI we might come to a different conclusion. The lowest blood sugar in Table VI corresponds to the highest lactating women and the three low lactating women are to be found among the four with the highest blood-sugar values, thus pointing to a connection between the extent of lactation and the level of the blood sugar. Such a conclusion could not be maintained in face of the evidence of Table VII nor from the general average figures of Table V. Such a demonstration illustrates, however, the danger of conclusion from a small amount of data. Indeed, in this connection we feel that the number of cases in our low and high lactating groups is small, and that we could not have drawn conclusions of a positive nature connecting the amount of lactation and the level of the blood sugar, even had our figures been in the right direction. It is only the fact that our blood-sugar values for the two extreme groups agree so remarkably well with our large average group, that makes us confident in drawing a negative conclusion. This lack of parallel in blood sugar variations between the lactation of woman and that of a highly specialized animal like the dairy cow may represent, however, no fundamental difference in the process itself. The difference may be merely that of degree. To what extent, then, does the milk yield of the group of high lactating women compare with that of the dairy cow? For purposes of comparison we may take Case H-r-f as shown in Table VII. This subject stands out over all the others as a milk producer. Her average production per

TABLE VI. SHOWING THE LACTATION OF A GROUP OF WOMEN OF BLOOD SUGAR RANGE 56 TO 75 MG. PER 100 C.C. PLASMA

SUGAR	2 HR. AVERAGE LACTATION	2 HR. AVERAGE LACTATION PER SQ. METER	LACTATION GROUP
mg.	c.c.	c.c.	
56	66	45.3	High
62	48	33.3	Average
68	67	39.8	Average
68	31	19.6	Average
72	5.6	3.8	Low
73	50	31.4	Average
73	0	0	Low
75	43	29.0	Low

TABLE VII. BLOOD SUGAR AND CALCIUM VALUES ON THE FIVE HIGHEST LACTATING WOMEN

SUBJECT	AVERAGE 2 HR. LACTATION	AVERAGE 2 HR. LACTATION PER SQ. METER	PLASMA SUGAR PER 100 C.C.	SERUM CALCIUM PER 100 C.C.
	c.c.	c.c.	mg.	mg.
K–k	106.0	63.0	86	9.8
O–l–r	101.6	65.1	88	9.9
Y–l	111.6	71.5	99	10.0
G–b–n	117.3	75.6	99	9.6
H–r–f	146.6	103.9	99	10.05

two hours per 1 sq. meter of surface was 103.6 c.c. of milk. Her daily output was 930 c.c. as measured on the tenth day. On a basis of weight, and allowing a figure of 400 kg. as the average weight of a cow, this woman would have put out 8 kg. of milk a day had she belonged to the bovine species. This is a small milk yield for a commercial animal (cp. the figures of Widmark and Carlens in Table II). The difference between the two species may then be found in the quantity of milk secreted, rather than in any fundamental difference in the process of lactation. Such a conclusion, however, possesses a corollary. It becomes extremely unlikely that we shall see in women any pathologic manifestation such as is seen in parturient paresis in cattle, and originating from the same cause. If parturient paresis in cattle is caused by excessive milk production, and the cause of the symptoms of convulsion and coma lies in a hypoglycemia, it becomes extremely unlikely that postpartum eclampsia in women (and this would be the nearest human analogy) owes its existence to a similar origin.

INSULIN AND LACTATION

Although our evidence is thus against any direct connection between the level of the circulating blood sugar and the level of lactation in women such as is claimed in cows, yet we felt our position would be more certain if we measured the milk output under experimentally produced fluctuations in the level of the blood sugar. Particularly

in view of the hypoglycemic theory of "milk fever" we have just discussed, we examined the action of insulin on lactation. Apart from the symptomatic observations of Widmark and Carlens, and of Auger on the effect of insulin on the cow, there appear to exist only two observations on the action of insulin on a normal lactating animal. The first of these is by Giush and Riotto[23] on the goat who found no effect. The second that of Banu and Heresco[24] who attempted to modify the lactose content of human milk by the injection of lactose, and the injection of lactone + insulin. In both cases the results were negative. Our own experiments are seventeen in number. The two hour lactation test was used as a standard, the average output of milk being noted. On the next morning 10, 15, or 20 units of insulin were given one hour before the beginning of the test. By this time the blood

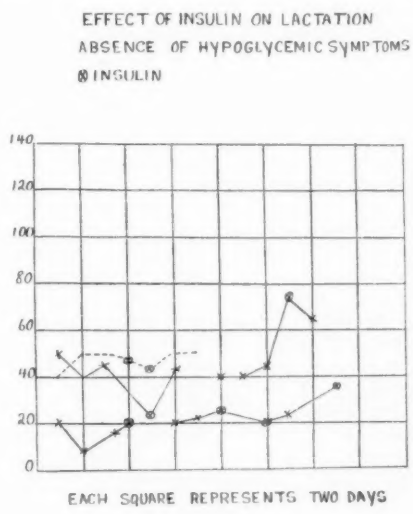

Fig. 3.

sugar level had been lowered, and we were thus able to observe the behavior of the gland when supplied with blood of a lowered sugar content. The blood-sugar level during the test and the occurrence of symptoms were noted. The results are presented graphically in Figs. 3 and 4. Our experiments are divided into two groups according to the presence or absence of symptoms. This is important as the mild symptoms following a low blood sugar (nervousness, tremors, perspiration, weakness) are symptoms of an emotional character, and we have previously discussed the effect on lactation of such simple procedures as the unaccustomed taking of a blood specimen, or the use of a breast pump. The production of emotional symptoms by the use of insulin then could not fail to be followed by a diminished milk flow. The correctness of this argument we think is illustrated in the experiments. Fig. 3 (experiments at-

tended by absence of symptoms) shows only one marked diminution in the two hour lactation test value. In two experiments the milk flow actually increased. In the remaining five the results lie within, or very near, the daily variation of the two hour test value. In this series of seven experiments, the lowest blood-sugar value was 53 mg. per 100 c.c. plasma with an average value of 65 mg. per 100 c.c. plasma. In Fig. 4 (experiments attended by presence of symptoms) are shown nine experiments, and each shows a distinct lowering of milk flow under the influence of the insulin. No increases are to be noted, though some of the decreases fall within the normal fluctuation. Four, however, are decreases outside the range of daily varia-

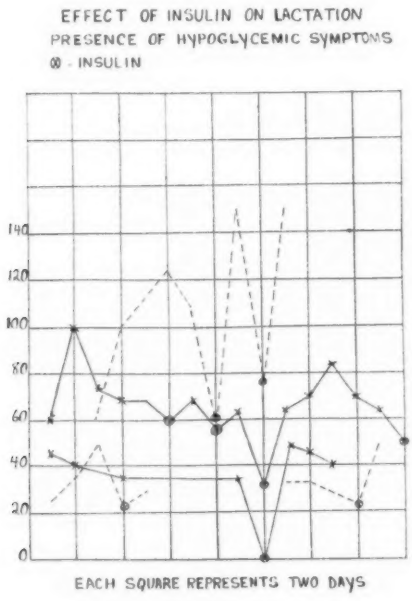

Fig. 4.

tion. One in particular shows a milk output of zero under the influence of insulin. This case showed the most marked reaction of all. The blood sugar fell to 48 mg. per 100 c.c. and a slight degree of cyanosis was noted as well as marked tremors and weakness. The average blood sugar of this group under the influence of insulin is 55 mg. per 100 c.c. plasma, a value lower than that shown in the cases of Fig. 3 but not sufficiently low to cause true hypoglycemic symptoms. Indeed, some of the symptoms were of the slightest, and would ordinarily have passed unnoticed had we not been particularly watchful. Nevertheless, even a slight headache, observed in two experiments corresponded to large downward fluctuations in milk output. The experiments we have just detailed may perhaps possess a bearing on the theory of the hypoglycemic origin of "milk fever" in cattle.

With the onset of even the mildest hypoglycemic symptoms, lactation should diminish. With the diminution in milk production should come a rise in the blood glucose, corresponding to the lessened strain on the carbohydrate balance. The condition should thus be self-limiting, or at least should show a greater percentage of natural recoveries than that of 50 per cent reported before the use of the Schmidt treatment. The answer to our criticism may perhaps lie in the fact that the great majority of cases of "milk fever" occur at the commencement of lactation, when perhaps the organism is not in a condition to adjust its carbohydrate balance with sufficient rapidity. On the other hand it is in primiparous cows that we should expect to see the greatest inability to adjust an unusual balance, as this would be the first time the mechanism is called into play, whereas the incidence of "milk fever" is highest between the fifth and tenth years. Moreover Greig emphasizes the occurrence of the same syndrome at any period of lactation.

PARATHYROID DEFICIENCY AND PARTURIENT PARESIS IN CATTLE

The theory of hypoglycemic origin of parturient paresis in cattle has not been received unanimously by veterinarians. Dryerre and Greig[25] have advanced a theory of guanidine intoxication due to parathyroid insufficiency. The analytic estimation of guanidine is a matter of much uncertainty at present, and figures in support of the theory are wanting. Moreover, the parathyroid deficiency as first proposed by Macallum and Voegtlin,[26] and later proved by Collip,[27] is accompanied by a lowered calcium percentage of the serum. Independently of the theory of guanidine intoxication, Little and Wright[28] struck by a similarity of symptoms between parathyroid tetany in animals and "milk fever" in cattle, suggested a lowered blood calcium as the origin of the convulsions of parturient paresis. They have published observations comparing the plasma calcium content of cows "down" with "milk fever" with the same animal on recovery. In every case the calcium is found to be markedly low when the animal is in the acute condition and raised to normal value on recovery. Moreover, it might be reasonable to expect the calcium exchange to be subject to strain at the beginning or during lactation. The negative calcium balance which most milking animals show is well known. Thus the hypocalcemia theory of parturient paresis would appear to have as much evidence in its favor as the hypoglycemia theory, though Little and Wright do not state whether the administration of parathyroid extract will bring about recovery.

Eclampsia in women has also had its etiology ascribed to a drain upon the calcium of the mother brought about by pregnancy.[4] The average blood calcium is perhaps very slightly lowered during the

latter months of pregnancy,[29] though the values remain within physiologic variation. Observations on the blood calcium during eclamptic seizures show normal values.[30]

BLOOD CALCIUM IN LACTATION IN WOMEN

Lactation in general does not affect the level of the blood calcium in animals, although it may unfavorably affect their calcium balance. Figures on the level of blood calcium in puerperium in women are scanty. De Wesselow[29] shows a slightly lowered range of calcium values from the third to the eleventh day postpartum, while Handelman, Rose and Sherwin[31] give slightly higher figures but still within normal variation. No figures are available connecting the serum calcium and milk production in women. We have, therefore, determined the serum calcium in the same series of women in whom we studied the blood sugar and classified our results in the same manner. The calcium was determined in serum by the method of Tisdall and Kramer.[32] The results are shown in Table VIII. The general average serum calcium value of 136 cases on the tenth day postpartum is 9.7 mg. The averages of the low, average, and high lactating women are 9.4, 9.7, and 9.7 mg. serum calcium: figures from which we could not possibly draw the conclusion that the production of a large amount of milk affected the level of the blood calcium. Table VII shows the

TABLE VIII. SHOWING LEVEL OF SERUM CALCIUM AND LACTATION IN WOMEN

LACTATION GROUP	NO. OF CASES	AVERAGE SERUM CALCIUM	RANGE SERUM CALCIUM	GENERAL AVERAGE CALCIUM
		mg. per 100 c.c.	mg. per 100 c.c.	mg. per 100 c.c.
Low	16	9.4	8.0–10.6	
Average	91	9.7	8.0–12.0	9.7
High	19	9.7	8.9–10.8	

serum calcium values of the five highest lactating women. The figures are within the usual normal range, and are a little above the general average. In Table IX are the lactation groups of all the women whose serum calcium ranged from 8.0 to 8.9 mg. per 100 c.c., i.e., slightly below the normal value. The lowest calcium values are found in women of the low lactating group. Indeed, if we considered the results in this table alone, we might draw the conclusion that it is the low lactating women who would be in danger of convulsions rather than the high lactating group, such as would be expected were the analogy between them and the parturient cow to be maintained. Such a conclusion, of course, is impossible in view of the general averages. It again emphasizes the worthlessness of conclusions drawn from a few experiments.

TABLE IX. SHOWING THE LACTATION OF A GROUP OF WOMEN OF SERUM CALCIUM VALUE 8.0 TO 9.0 MG. PER 100 C.C.

CALCIUM	2 HR. AVERAGE 2 HR. AVERAGE LACTATION	2 HR. AVERAGE LACTATION PER SQ. METER	LACTATION GROUP
mg. per 100 c.c.	c.c.	c.c.	
8.0	0.0	0	Low
8.0	5.6	3.8	Low
8.0	7.3	5.0	Low
8.0	15.0	8.4	Low
8.0	50.0	31.4	Average
8.5	18.3	12.5	Average
8.6	18.3	12.7	Average
8.7	30.0	28.0	Average
8.8	55.0	32.5	Average
8.9	51.6	31.4	Average
8.9	15.0	10.1	Average
8.9	88.3	56.2	High
8.9	81.6	55.1	High

PARATHYROID EXTRACT AND LACTATION

The power of extracts of the parathyroid gland to raise the level of the blood calcium in the dog and in man is now a well accepted fact. Even apart from the possibility of a relationship between hypocalcemia and "milk fever" it would be of interest to observe the effect of a raised serum calcium on the milk output. There appear to be no observations in the literature. We have made observations in two cases. Collip's parathyroid extract (Para-thor-mone, Eli Lilly Co.) was given in the doses shown in Table X to two cases. The effect on the lactation in S-n-n is negative. In G-n it might appear that there was a gradually increasing lactation due to the parathyroid extract. The baby in this case, however, had just been changed from a four hour feeding to a three hour feeding owing to its lack of gain of weight. This would constitute an extra stimulus to milk flow, and in view of this, we feel we cannot argue that the parathyroid extract was responsible. We should like to point out the difficulty we experienced in raising the serum calcium in both these cases. Subject G-n received 40 units a day for three days and 80 units on the succeeding day. Yet the calcium never rose above 11.03 mg. The blood, however, showed a marked anhydremia. The patient felt very nauseated, had a dry mouth, had excessive thirst, and as she herself expressed it, "felt dopy and miserable." These symptoms were alleviated on the next day with the copious administration of fluids. Collip and others have reported acidosis and dehydration in dogs to whom parathyroid has been given in excessive amount. In Collip's report the symptoms followed a hypercalcemia of 14 or 15 mg. Although no such hypercalcemia was observed in our subject we believe that the symptoms were those corresponding to parathyroid excess in dogs, though no acidosis symptoms were noticed. Two days afterwards the subject

developed a temperature with general pains which was diagnosed as a mild influenza attack. No temperature was noted during the anhydremic period. If our conclusions are correct this forms the first record of symptoms occurring after the use of parathyroid extract in the human subject. Subject S-n-n also showed the symptom of headache after 60 units for two days. The anhydremia on the following day was not so marked as in the previous case. The calcium rose to 11.38 mg. It would appear that the administration of parathyroid extract in the lactating human subject is not without its dangers. Although we feel we cannot conclude the presence of a direct connection between parathyroid extract and milk flow yet it must be remarked that symptoms, exceeding in severity many of those experienced by our insulin subjects did not produce a decrease in the two hour lactation test.

TABLE X.—SHOWING THE EFFECT OF PARATHYROID EXTRACT ON LACTATION

SUBJECT DATE	PARATHYROID EXTRACT	SERUM CALCIUM	SERUM PROTEIN	TWO-HOUR LACTATION	NOTES
1925	UNITS	MG. PER 100 C.C.	PER CENT	C.C.	
G – n					
Dec. 15	10	10.4	8.66	40	Baby on three-hour feeding
" 16	40	10.5	8.06	50	
" 17	40	9.8	7.95	55	
" 18	40	10.3	7.96	50	
" 19	80	11.0	8.02	55	Nauseated A.M.
" 20	0	10.8	9.18	60	Dry mouth, thirsty, miserable
" 21	0	10.6	8.00	60	Improved
" 22	0	9.7	7.50	65	Temperature 100°
" 23	0	9.3	7.24	65	Improved
" 24	0	–	–	45	Well
1928					
S-n-n					
Jan. 23	0	9.5	7.85	45	Baby on four-hour feeding
" 24	0	–	–	65	
" 25	0	–	–	60	
" 26	0	10.0	7.20	60	
" 27	0	–	–	70	
" 28	0	–	–	75	
" 29	30	10.2	7.20	70	
" 30	50	11.4	7.30	50	
" 31	0	11.3	8.25	60	Not feeling well
Feb. 1	0	10.1	6.98	45	Slight temperature

We wish to express our indebtedness to Messrs. Eli Lilly Co., for the "Para-thormone" used in these observations.

FINDINGS IN A CASE OF PUERPERAL SEPTICEMIA

The evidence as we have interpreted it is against any analogy being found between "milk fever" in cattle and a corresponding state in woman if either a hypoglycemia or a hypocalcemia be accepted as a fundamental accompaniment. Either the endocrine balance in woman is more flexible than in the cow, or as we have stated, the amount of lactation in woman never rises to such an excessive amount

as to disturb the balance. It may be objected, however, that all our experiments are on the tenth, eleventh, and twelfth day postpartum, a time when lactation is well established, and any disturbance may be adjusted. We have pointed out that lactation in the dairy cow lowers the blood sugar quite apart from the immediate puerperal period, and that some veterinarians, as stated by Greig, believe that "milk fever" can occur at any period of lactation, though it usually occurs forty-eight to seventy-two hours after labor. In view, however, of this possible criticism, we have made a daily blood examination for sugar and calcium on five subjects for a period of six days, commencing the first morning after labor. These are shown in Table XI. Incidentally the table shows the N.P.N. and amino-acid N values,[33] as these values appear of importance in one case (A-r). These and other values were

TABLE XI. SHOWING DAILY VALUES AFTER LABOR OF N.P.N. AMINO ACID N., CALCIUM AND SUGAR IN BLOOD

DAY AFTER LABOR	1	2	3	4	5	6
			N.P.N. mg. per 100 c.c. Plasma			
Y – g	31	–	28	25	25	23
S – r	35	30	29	24	24	24
R – m	25	23	23	20	21	22
R – s	24	22	22	20	23	20
A – r	32	40	50	24	20	22
			Amino N. mg per 100 c.c. Plasma			
Y – g	4.8	5.2	4.5	5.0	5.3	5.1
S – r	4.8	5.5	5.3	5.1	5.4	5.8
R – m	5.4	5.6	5.5	5.2	5.5	5.6
R – s	5.0	5.2	5.3	5.5	5.2	4.7
A – r	6.1	6.0	7.8	5.0	5.1	5.5
			Calcium mg. per 100 c.c. Serum			
Y – g	9.6	10.0	10.4	9.6	10.0	9.8
S – r	10.4	10.6	10.0	10.2	10.0	10.7
R – m	9.4	10.1	9.4	9.8	9.7	10.1
R – s	10.1	9.6	9.5	8.9	9.9	9.9
A – r	10.0	10.2	8.8	9.1	9.0	9.0
			Sugar mg. per 100 c.c. Plasma			
Y – g	92	98	83	98	86	95
S – r	87	87	97	83	88	98
R – m	85	88	88	89	90	92
R – s	76	79	81	83	80	85
A – r	97	92	100	115	102	96

determined in all cases studied but are not included in this paper as they are not pertinent to the particular phase of the subject under discussion. The figures show no remarkable or characteristic variation due to the onset of lactation. Case Y-g belonged to the low-lactating group and R-n to the average-lactating group. The interest of the table lies in subject A-r who on the third day showed a moderately raised N.P.N. of 50 mg., a high amino-acid N of 7.8 mg. and a sudden drop in the calcium to 8.8 mg. Whether the rise in sugar to 100 mg. is part of the same disturbance we do not know. The rise in N.P.N. and amino-

acid N are outside the normal fluctuation. Of nearly 130 cases, studied on the tenth day postpartum, only 3 show amino-acid N values of 6.0 mg. or over. The disturbance is evanescent. On the next day all that is left is a slightly raised blood sugar, but even so, this figure would be accepted as within the normal range. The disturbance was probably due to the onset of a mild puerperal infection as it was accompanied by a temperature, and a culture of streptococcus hemolyticus was obtained from the cervix. The temperature was normal the next morning, though occasional rises were noticed later. The occurrence of a sudden drop in calcium in this case on the third day postpartum presents the only analogy we have been able to find between "milk fever" in cattle and pathologic postpartum disturbance in woman, a disturbance much more likely due to infection rather than to lactation. In view of the markedly pathologic value of amino-acid N we have found, it would be interesting to know the value found in parturient paresis in cattle, especially as the effect of lactation in the cow is to produce a low value. In man it is extremely difficult to find examples of disturbance in this substance in the blood.[34]

GENERAL CONCLUSIONS

If parturient paresis in cattle is fundamentally attended by either of the biochemic phenomena discussed in this paper, it appears very unlikely that its analogue will be discovered in woman. Such a conclusion is based upon the hypothesis that excessive milk production is an essential condition of parturient paresis, a hypothesis accepted by all veterinarians as far as we are aware. That even high lactating women do not attain that plentitude of production reached by dairy animals may perhaps represent the difference between the two species, as we have suggested. Nevertheless it seems strange that no trace of the disturbance can be found in women, so strange that it may engender doubts as to the fundamental nature of either the hypoglycemic or hypocalcemic theory of the pathologic manifestations in cattle.

SUMMARY

1. The recent theories of parturient paresis in cattle are discussed in the light of a possible relationship to similar disturbances in women.

2. A lactation test of two hours' duration has been devised for women, and its relationship to the twenty-four-hour output of milk has been studied.

3. Seventy-one per cent of the women examined secrete 10 to 40 c.c. milk per square meter of surface per two hours. This constitutes the average lactation group.

4. Only 15 per cent of women secrete over 40 c.c. milk per square meter of surface per two hours, constituting a high lactation group.

5. There is no essential difference in the blood-sugar level of the three lactation groups, the average figure being 95 mg. per 100 c.c.

6. Hypoglycemias produced by insulin lower the milk output, if the hypoglycemia is accompanied by nervous or emotional symptoms.

7. The average serum calcium level for 136 cases is 9.7 mg. per 100 c.c.

8. There is no essential difference in the level of serum calcium between the three lactation groups.

9. The administration of parathyroid extract has no influence on the milk production.

10. It appears difficult to raise the serum calcium by parathyroid extract during lactation.

11. Toxic symptoms have been noted by the administration of parathyroid extract to a human subject.

12. Some abnormal chemical findings are reported in a case of puerperal septicemia.

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REPEATED LAPAROTRACHELOTOMY, 91 CASES*

(Low, or Cervical Cesarean Section)

By Joseph B. DeLee, M.D., Luella E. Nadelhoffer, M.D., and J. P. Greenhill, M.D., Chicago, Ill.

AMONG the seventeen superior advantages possessed by the low, or cervical operation, two are always mentioned as being of such importance that they alone should induce all thinking accoucheurs to adopt the cervical approach to the uterus for all cases requiring abdominal delivery.

The displacement of the classic operation by laparotrachelotomy is proceeding so rapidly all over the world, and the operation has been adopted as standard by so many obstetric authorities, that one must conclude its primary mortality and morbidity are now proved to be better than all other methods of cesarean section.

It remains, therefore, to discover the facts regarding the late mortality and morbidity, that is, how women who have had one cervical cesarean get along afterward, whether the fear of abdominal delivery restricts future childbearing, or whether the incised uterus becomes sterile, also how the uterus acts in subsequent pregnancies and labors, and what are the findings at subsequent operations.

We have tried to follow up the cases on whom the laparotrachelotomy has been done, but the moving qualities of our population have prevented us from learning much of value. One may surmise, from the fact that few of the women have returned to us for gynecologic treatment and still fewer have responded to the questionnaire we sent out to them, that the low section does not compromise their health.

The exact effect of the operation on fertility could not be determined, but since we are able to present 91 cases of repeated section it shows that this element does not act very strongly inhibitive.

The two advantages of the low cesarean above referred to are the integrity of the uterine scar and the absence of abdominal adhesions. The health of the women, fertility, their safety in pregnancy and labor, all depend on these two factors and from a study of our 91 cases we may deduce practically valuable facts.

The statistical material used in this paper was collected, tabulated, and abstracted by my associate Dr. Luella E. Nadelhoffer, and the microscopic study of sections of the cervix, removed at operations, was done by my associate Dr. J. P. Greenhill, to both of whom should go the credit for the much greater work done. All I did was to as-

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semble the information brought to me by them and make a few general comments. Only a small portion of their findings are presented here.

Of these 91 cesareans I performed 31, my 8 associates the other 60.

In 718 cases of laparotrachelotomy, 82 were done for the second time, 8 for the third, and one for the fourth time.

TABLE I

INDICATIONS FOR FIRST SECTION	NO.	PER CENT
Contracted Pelvis	69	83.1
Toxemia	6	7.2
Abruptio Placentae	2	2.4
Placenta Previa	1	1.2
Fibroid Uterus	1	1.2
Amputation of cervix	1	1.2
Cardiac defect	2	2.4
Threatened rupture of uterus	1	1.2
	83	

The indications for the first laparotrachelotomy were mainly contracted pelvis, 83.1 per cent (Table I) and naturally the indication was carried over into the second pregnancy. The fact of there having been one incision in the uterus already would strengthen the indication for a second section although I believe, and most men doing the low operation insist, that this element of danger requires much less consideration than does the scar after the classic section.

TABLE II

INDICATION FOR FIRST CESAREAN SECTION		INDICATION FOR SECOND CESAREAN SECTION
Toxemia	(6 cases)	1. Toxemia again 2. Toxemia again 3. Cephalo-pelvic disproportion 4. Threatened rupture of uterus—in labor eight hours 5. Elective 6. Threatened rupture of uterus
Abruptio Placentae	(2 cases)	1. Forty-eight hour test of labor 2. Elective
Placenta previa	(1 case)	Elective
Fibroid Uterus	(1 case)	Same indication
Amputation of cervix	(1 case)	Same
Cardiac defect	(2 cases)	Same
Threatened rupture of uterus	(1 case)	Elective

All the patients who had third cesarean sections had contracted pelves, also the patient on whom the fourth section was done.

Table II shows the indications for the second section when the first was not done for contracted pelvis. Toxemia recurred twice, and in two cases a rupture of the uterus was feared.

TABLE III. TIME INTERVAL BETWEEN FIRST AND SECOND CESAREAN SECTION

	NO.	PER CENT
1 to 1½ years	13	15.7
1½ to 2 years	11	13.3
2 to 2½ years	17	20.4
2½ to 3 years	11	13.3
3 to 3½ years	10	12.0
3½ to 4 years	9	10.8
4 to 4½ years	4	4.8
4½ to 5 years	5	6.0
5 to 5½ years	1	1.2
5½ to 6 years	1	1.2
7 to 7½ years	1	1.2
	83	

TABLE IV. TIME INTERVAL BETWEEN FIRST AND SECOND AND BETWEEN SECOND AND THIRD CESAREAN SECTION

	FIRST AND SECOND	SECOND AND THIRD
11 months		1
1 to 1½ years	2	4
1½ to 2 years	1	1
2 to 2½ years	2	
2½ to 3 years	1	
3 to 3½ years	1	1
4 to 4½ years	1	
4½ to 5 years		1
	8	8

TABLE V. FOURTH CESAREAN SECTION, TIME INTERVAL BETWEEN

First and second	1½ years
Second and third	1½ years
Third and fourth	3½ years

Tables III, IV, and V, show that the interval between the several sections varied from one to seven and one-half years, 40 women having a second child within two and one-half years. This is a large percentage (51.3 per cent) and is slightly greater than the percentage of second births of 100 women taken at random from the hospital files (50 per cent). It is generally admitted that a relative sterility remains after the classic cesarean. In eight of the third cesareans 6 of the women had conceived within one year after the second operation. As far as sterility is concerned we cannot say that laparotrachelotomy restricts it very much, and this is a strong argument for the cervical operation.

The youngest patient on whom the section was repeated was twenty-one, the oldest forty. In all patients the pregnancies were at or about term. Since the second cesarean was nearly always foreseen, a large percentage were elective, i.e., nearly 60 per cent, but the rest were given a test of labor lasting from one to forty-six hours, the majority

having less than twelve hours of pains. In these patients it was possible to see the effect of labor on the lower uterine segment and scar.

Local anesthesia was the anesthetic of choice and was successful in 60 per cent of the cases, ether being next with 33 per cent; combinations being used in the remainder. Of late years we are learning how to treat the minds of our patients better, and the local method is now being found practicable in more than 90 per cent of operations, and even for Porro.

Sterilization was performed after the second section whenever the patient and her husband desired it, and we have finally, after much experimenting, adopted the simple method of Madlener. Thirty-one of the 91 patients were sterilized.

In the 718 laparotrachelotomies there were 9 maternal deaths, 1.2 per cent. One woman died after her second operation. One died after her third, a total mortality of 2.2 per cent in the 91 repeated sections. Of the babies 4 died, one a monstrosity (anencephalus), one from atelectasis (the child of the mother who died after the third section) and one from sepsis, probably umbilical, one from infection acquired before labor.

The first mother who died weighed over 280 pounds, entered the hospital in labor with a foul discharge, the bag of waters having ruptured two days before. The child when delivered had a purulent discharge from the nose and a temperature of 102°. It died of sepsis the fourth day. The uterus was foul at the operation. Death was due to peritonitis which probably came from the uterus, although some of the symptoms pointed to the gall bladder. The second death was most peculiar and presents many interesting aspects. During her first pregnancy this patient suffered from anemia whose nature was not determined by the internist. She was of the hypoplastic type, enteroptotic, flabby, with weak mesoblastic tissues. Her abdominal walls were so thin that the uterus could be seen through it. Her first labor dragged on for several days. Laparotrachelotomy was performed. On the thirteenth day fever of 103° appeared and, since there were no lochia, we diagnosed retention and passed a soft catheter into the uterus, nothing came out, but the patient very soon afterward developed double phlegmasia alba dolens. Recovery after two months.

During her second pregnancy the anemia reappeared and a new symptom, uterine contractions simulating labor pains, and requiring narcotics. These kept up from the end of the sixth month into the eighth giving some concern as to the integrity of the lower uterine segment scar, and also for the baby's life. When the child was appraised at 5½ to 6 pounds a second laparotrachelotomy was performed. The baby weighed 5¾ pounds and died in six hours of atelectasis pulmonum. The mother became enormously distended,

without fever, had stercoraceous vomiting for twenty-four hours, but recovered. I warned her not to get pregnant again, but she did and had a spontaneous abortion at three months. Not long thereafter she reappeared, now at the seventh month of gestation with only mild uterine contractions. At term the bag of water ruptured and a few pains occurred. Since the pelvis was slightly justo minor, the head high, occiput posterior, the cervix closed, a third laparotrachelotomy was performed. The scar was very thin but firm. A large, fine boy was delivered. There was a great deal of venous oozing from the wounds, and especially did we have trouble stopping the hemorrhage from the right tubal corner when we resected the tubes to procure sterilization. Her recovery began like the second one, distension, vomiting, not fecal this time, but more obstinate. She had little temperature, pulse of 90 to 110 and slow respiration, her white blood count was 7000 to 5000. A consultation of surgeons could not diagnose peritonitis but when we reopened the abdomen this was found, and it seemed to take its origin from the right tubal corner. I have noticed that our cesareans that have any manipulations on the tubes have more reactions than the others, and believe we probably stir up an infection slumbering in this neighborhood. The other patient who died was also sterilized.

The recovery of the other 89 women was just as smooth as usual, if not better. Primary union took place in all but 4 cases, and pelvic cellulitis was noted twice; 55 per cent had normal temperature.

Intestinal complications, gas pains, distension were noted as severe in 4 cases, mild and temporary in 44 cases; vomiting occurred only in 13 cases and was not marked. One patient on the day she arrived at home had a severe pulmonary embolism but happily recovered. In her case the transverse incision was made and bleeding at the outer angles of the wound required numerous sutures.

The behavior of the cervix in subsequent pregnancy and labor presents little of importance in this discussion.

Of 48 women who could be followed up, menstrual disturbances not existing before were found in 10; one woman had profuse menses; 44 had regular periods, 3 irregular, 1 none at all. Forty-four patients nevertheless said they felt "very well." While the dysmenorrhea was not pronounced, its occurrence is interesting.

One patient complained of bladder disturbances, 2 of backache.

That fertility is little interfered with is shown by the fact that we were able to do 91 repeated sections in a total of 718 cases. Pregnancy after the first section did not present anything unusual. Four abortions were reported in women who had had one laparotrachelotomy which is not a remarkable incidence. Out of 136 classic sections done during the same period, 4 women had abortions, proportionately 5 times as many.

Premature labor was not noted, indeed several of the women went over term. There was no case of rupture of the uterus either during pregnancy or labor. Even the patient with the thin scar above referred to did not give any concern.

At least twelve women, after previous laparotrachelotomy, have been delivered from below, some spontaneously and others by forceps. In one case labor was induced by bag. Labor lasted from two to thirty-five hours and in many cases the pains were very strong. The babies weighed from 2500 to 4255 grams. One patient had two vaginal deliveries after laparotrachelotomy and another patient had two vaginal deliveries after two laparotrachelotomies. All this speaks well for the integrity of the cervical scar, although anatomically, as Dr. Greenhill shows, much is to be desired in the restoration of tissue.

Of special interest are the findings at the second laparotrachelotomy. No unusual difficulties were encountered in opening the abdomen. One hernia was met. Adhesions were found in 40 per cent of the cases but they were mostly very thin and easily treated. They were between the uterus and omentum, abdominal wall or omentum, or between peritoneum and uterus. Of the 8 third cesareans 5 had adhesions but the woman who had a fourth laparotrachelotomy had no adhesions at all. In 2 cases expansive gauzy adhesions made it possible to do the second trachelotomy extraperitoneally. I have met with adhesions after the classic section, where they occur in 85 per cent of cases and are dense, often intestinal as well as utero-abdominal. There is no comparison between the two cases. All the advantages are with the low operation, as far as adhesions are concerned.

The bladder is separated from the lower uterine segment with a little more difficulty in the second sections. The histories are incomplete on this point. My memory says that the frequency of firm bladder adherence to the uterus is not great nor the complications at all hard to overcome. The location of the bladder requires some consideration. Since the majority of repeated sections are elective, and labor pains have not unfolded the lower uterine segment the bladder is usually low in the pelvis, unless it was elevated by the first operation. When we were overlapping the peritoneum in the two flap operation, it was not uncommon to find the bladder fixed high on the uterus and also drawn up out of the pelvis permanently, being elevated also on the anterior abdominal wall. In 78 cases the bladder is recorded as high in 39, low in 36 and normal in 3. These figures are about what we find at first sections and, therefore, mean little.

The records are incomplete as to the quality of the uterine scar. Of 29 cases it was mentioned as thick in 18, thin but strong in 3, thin in 3, not seen but felt in 4, and separated in one (previously mentioned).

Dr. J. P. Greenhill studied 40 pieces of the lower uterine segment

removed at the time of the second laparotrachelotomy and presents herewith a preliminary report on 31 specimens. In 5 of the 40 he reports thin scars.

Histology of Uterine Scars.—(J. P. Greenhill, M.D.) In 31 instances at the time of the repeated cesarean section, pieces of tissue were removed from the site of the previous incision in the lower uterine segment. In addition, pieces of tissue were removed from three uteri at the time of a first operation for purposes of comparison.

In 26 of the 31 specimens studied there were distinct evidences of scarring. The remaining five blocks failed to show any scar tissue whatever. This means that in these five cases the incision healed perfectly or that the pieces of tissue were not removed from the site of the former operation or operations. For at the time of a repeated low cervical cesarean section it is unusual to recognize the site of the previous incision with the naked eye before incising the lower uterine segment. The remaining 26 specimens in which scarring was present can be roughly divided into three groups, depending on the degree of scarring. In three cases, the changes were striking, consisting essentially of marked thinning of the uterine wall and replacement of a great deal of muscle tissue with fibrous tissue. In each of these specimens the wall of the uterus contained a sharply localized area of constriction, so that the wall measured less than a third of a low powered microscope field in thickness. In two of these, this portion of the wall was made up of approximately equal parts of muscle and fibrous tissue, but in one the muscle tissue had been almost completely replaced by collagen and a small amount of elastic tissue. Large amounts of fibrous tissue extended outward into the normal myometrium. Into these scars the endometrium and parametrial tissue were sharply drawn. In none of these sections was there any evidence of disintegration of the wall of the uterus, as was suggested in some of the scars described below.

In the second group were placed those cases where undoubted scars of the old incisions were present, but in which the integrity of the wall remained essentially unchanged, even though several showed slight thinning of the wall. Most of these scars were composed of dense masses of fibrous tissue frequently arranged cicatrically. Others contained various amounts of muscle tissue bundles and individual cells, many of which were surrounded by collagen. In a few instances the scarring was extensive, reaching from the endometrium to the parametrium and involving large areas. In many specimens large interstitial areas of diffuse, irregular scarring were present. Most of these scars were represented by fibrous tissue replacement but there were a few in which the tissue, although arranged irregularly with a tendency toward cicatrization, was mostly muscular. A number of the fibrous scars contained dense masses of elastic fibrils, others were

found with diffusely scattered elastic tissue and some were almost entirely free of elastic tissue. No factors governing the formation of elastic tissue were determined, but there did not seem to be any relationship to the amount of collagen. Several dense scars had large amounts of coarse elastic fibers; other equally dense scars were relatively free from it. It is possibly of some significance that, in general, those scars which consisted of dense masses of fibrous tissue showed, within the scar proper as well as in the adjacent myometrium, marked edema of the fibers so that in places isolated muscle cells were imbedded on a pale-staining, very loose, edematous, fibrous tissue network, giving the impression of early "tearing" of the tissue. This group included 15 cases, one of which could conceivably fall into the first group.

The remaining cases, eight in number, showed minor degrees of scarring of the same general type. The one with the least evidence of scarring contained only two small puckered areas, one of muscle and the other of collagen, both areas being interstitial. The lesions of this group were of microscopic size, and are thought to be of purely anatomic rather than physiologic significance.

While looking for scars in these tissues, we found two cases with distinct acute inflammatory reactions, diffusely involving the endometrium and subjacent myometrium. These reactions consisted of edema and especially in one case, of marked leucocytic infiltration. No relationship to blood vessels was noted, the process being a diffuse one involving the inner surface of the uterus. No bacteria were seen in the sections. One of the patients from whom a piece of tissue was removed had no labor pains when the cesarean section was performed and the other had been in labor two hours. In both cases the bag of waters was intact at the time of operation.

These sections were stained with hematoxylin and eosin, and by the Weigert-van Giesen method, in which nuclei stain blue, muscle tissue greenish-yellow, collagen red, and elastic fibers black. This study is being continued.

The scars were found thin in many cases yet they held throughout pregnancy and more or less hard labor. In only the one case the peritoneum seemed to lie on the decidua, and in all probability this lower uterine segment would have ruptured had much of a strain been put on it.

Dr. Greenhill is making a further study of the microscopic slides and the clinical records with a view of determining whether the method of suturing, continuous or interrupted, has anything to do with the resultant scar. Thus far it seems to be proved that thin scars oftener follow continuous suturing. I have been practicing and teaching the interrupted suture of the lower uterine segment for the last four years, basing my opinion on my own findings at operation. Now a pathologic foundation is placed under it. The interrupted

suture takes longer, and the patient loses more blood while it is being put in. Where haste is needful because of hemorrhage, one may compromise and put in one row or part of one, continuous and finish the closure with interrupted.

It seems that perfect anatomic restoration of the cervix is not necessary for the strain of subsequent labor. All that is needed is a good scar. In the world's literature there are only 12 cases on record in which rupture of the cervical scar took place. All these women were in strong active labor and only two of the mothers died. Compare these figures with those of the classic section, with its high percentage of ruptures during pregnancy, when the patient is usually at home without any warning, such as labor pains give; also note the still higher percentage of rupture during labor, and a large mortality in both.

I have always put forward that the laparotrachelotomy is not as simple an operation as the old classic, that it usually presents only such difficulties that an ordinarily skilled abdominal operator can master with ease. We must not forget that occasionally a classic section will also have complications, especially if it is a repeated one, that will tax the surgeon's skill, and the same is true of the repeated low cesarean. In all cases of primary and second laparotrachelotomy, the technic is easier if the patient has been in labor a moderate length of time because then the lower uterine segment is long drawn out and thin, and the bladder separated from it. These advantages are absent with repeated section which is almost always an elective operation. Occasionally if labor has not supervened and the lower uterine segment has not unfolded well one has to extend the incision one to three centimeters upward into the corpus uteri. The two instances in our tables where the cut was made longer (up to 2 inches), were *lapsi artis.* No harm results from this as the whole incision can be well peritonealized, and if a second or third elective section is to be done, there is no danger from rupture of the scar as with the low incision this only occurs after prolonged and powerful labor.

In all second laparotomies care is necessary in opening the abdomen, as an occult hernia may exist. Adhesions are seldom met, as was said, but one must be prepared for an elevated bladder. The peritoneal opening, therefore, must be made at the upper end of the incision. The anterior culdesac, especially if the overlapping of the 2 peritoneal flaps was extensive may be very high and distorted. Adhesions, if the previous section was a classic may twist the uterus, if a low operation, this is rare. Where the healing of the first section was afebrile, one need not fear that the separation of the bladder from the lower uterine segment will be difficult. If suppuration occurred, one must proceed carefully with the dissection. We have not injured the bladder in any repeated operations nor have we tied or

cut the ureter. Uretero-pyelitis is noted as a complication in the recoveries from laparotrachelotomy in about 3 per cent. This is due to two causes, first we perform this operation frequently in threatened eclampsia, and toxemia is often the result of this inflammatory underlying disease; second, when the bladder and the ureters are lifted off the lower uterine segment, the disturbance may light up a slumbering infection. There was only one case of cystitis in this series of repeated sections.

Really there is little to say about the technic of a repeated laparotrachelotomy. It is usually just like the first one and when it is not, general surgical principles apply.

Should one sterilize the woman after her second abdominal delivery? Yes, if she and her husband demand it, although I usually dissuade them from such a course. I do not try to dissuade them after a third section. If the patient is well on in years, a Porro is probably the best way to sterilize. In young women Madlener's method, simple and efficient, can be done. A loop of the tube is held up, crushed carefully with a heavy forceps and a silk ligature laid in the groove.

In closing the abdomen the interrupted suture is used throughout because scar tissue does not unite as well as healthy, and a continuous suture compromises the circulation too much.

Altogether, a second laparotrachelotomy is not quite as easy as the first, but this is true of all second laparotomies.

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SALPINGITIS: THE CASE FOR EXPECTANT TREATMENT

By C. Jeff Miller, M.D., New Orleans, La.

AS HOWARD KELLY once remarked, surgery developing in the hands of men has dealt too lightly with mutilating operations in women, and if the case might be reversed for several decades, with women operating and men suffering the mutilation, there would undoubtedly be a large prepossession in favor of wise conservatism. His point is well taken. Since the ablation of the female sexual apparatus is not ordinarily a procedure which endangers life, there is a tendency, unfortunately a somewhat general tendency, to remove it, in whole or in part, on indications which, in another part of the body, would be considered rather trivial. Function is lost sight of, sentiment is thrown to the winds, and unnecessary and mutilating surgery is done without a consideration of equally satisfactory and more conservative modes of treatment, without a recollection of the fact that a woman's whole scheme of life takes its point of departure from her pelvic

organs. If that one point alone were borne in mind, a new day would dawn in the management of many types of pelvic pathology.

Almost twenty years ago F. F. Simpson read before the American Gynecological Society a paper which revolutionized the treatment of tubal disease. Prior to that time its management had been purely surgical. Operation was done routinely, as soon as the diagnosis was made, and because it was done in the acute stage, ablation of the entire genital tract was often a necessary consequence. The result was not only a group of thoroughly unsexed women, at least in the physiologic sense, but also a death rate approaching 20 per cent. Then came Simpson with his advocacy of the delayed operation, with the plea that surgery should never be resorted to in acute salpingitis until the temperature had been consistently normal for at least three weeks, even after repeated bimanual examination, until there had been absolute recovery from the acute attack, and until there had been a complete absorption of the inflammatory exudate surrounding the primary focus of infection. These astounding proposals could not be ignored, revolutionary as they were, because their advocate was able to show for them in a series of more than four hundred cases the hitherto unheard of mortality of 1 per cent.

Almost from that day the accepted treatment of acute salpingitis has been medical and not surgical, but in spite of the proved results of the delayed operation, there are still those who advocate a return to the old plan of immediate surgery. The fact that the majority of these men are brilliant and expert surgeons makes their arguments particularly dangerous. Their individual results, I grant you, are striking, but we must not lose sight of the fact that the bulk of all surgery is done not by surgeons of this eminence but by men of average ability, or, to speak bluntly, of small ability, whose disregard of established principles may have a very different outcome.

Salpingitis, you will recall, is essentially a bacterial invasion of the fallopian tubes in which practically any organism, either singly or in combination, may be the responsible factor. While it is generally conceded that at least 70 or 75 per cent of all cases are of gonorrheal origin, laboratory confirmation is possible only in a relatively small percentage of these. The gonococcus is an organism which cannot exist without oxygen, and once it has become encapsulated in the tube, death is inevitable and activity ceases. Clinically this process is accompanied by a fall in the temperature, the gradual absorption of the inflammatory exudate, and finally the complete recovery of the patient from the acute attack. The correspondence between the recession of the bacterial activity and the clinical improvement is indisputable, and Curtis makes the unqualified statement that in all his experience he has never isolated the gonococcus from the secretions of patients

who either failed to reveal gross evidence of active inflammation or who had been free from fever for a minimum of ten days. It is his opinion, therefore, that persistently active tubal disease is not, as it has long been regarded, a chronic condition with acute self-originating exacerbations, but rather either a fresh infection from without or a fresh extension upward from a chronically infected lower genital tract.

With the nonspecific organisms the situation is somewhat different. The acute attack tends to subside, the exudate tends to be absorbed, exactly as when the specific organism is present, but the nonspecific organisms are anaerobic, and they therefore, although quiescent, have in them decided potentialities for harm for unknown periods of time. Their longevity has never been definitely limited and the streptococcus, at least, has been isolated from the tube as late as nineteen years after the original attack.

From these facts and from studies of the clinical findings in literally thousands of cases of tubal disease, certain indisputable conclusions emerge. Salpingitis, at least of the specific type, tends to recede spontaneously from the acute stage; that is, autosterilization tends to occur and the woman develops her own immunity and can protect herself against the bacterial invasion which has taken place. In the nonspecific type spontaneous regression is likewise the rule, though the organisms retain their activity for unknown periods of time. In the second place, spontaneous clinical recovery must be considered at least a possibility in every case of salpingitis, though naturally it is more frequent in the mild than in the extremely severe type. In the third place, involvement of the general peritoneal cavity is exceptional and death during an acute attack is equally unlikely.

These are proved clinical facts, the acceptance of which carries the corollary that the factor of safety cannot enter into the plea for immediate operation. The patient, other things being equal, will not die because operation is withheld, and the case for prompt surgery must, therefore, be argued on some other premise. Certain arguments may be promptly demolished. Thus salpingitis is not comparable to such a condition as appendicitis, where delay would be fatal. The diagnosis is usually so clearcut that it can seldom be confused with other abdominal pathology in which prompt surgery is essential. Rupture of a pus tube is an unlikely contingency; in fact, the few cases in which this catastrophe has occurred are reported in the literature almost as surgical curiosities.

Moreover, the other side of the picture must not be forgotten. It must be borne in mind that immediate operation is done in the face of active bacteria, in the face of fresh adhesions, in the face of structures so vascular, so infiltrated and so friable that they may be injured by even the gentlest manipulations, while the delayed opera-

tion is done when the bacteria are dead, when the pus collections are sterile, and when extensive contamination of the field of operation with resulting peritonitis is not so likely to occur. Another consideration not to be ignored is whether a patient already acutely ill from a bacterial disease is in a condition to stand the added strain of surgery since, and this is the crucial point, her life, as we have already shown, does not hang upon its prompt performance. Moreover, it must never be forgotten that surgery, when it is done, is done for the *results* of the acute attack, not for the attack itself, which may subside spontaneously and which may leave no secondary pathology, so that routine operation for a condition which at least in a certain percentage of cases, will be cared for by nature rather than by art, can be classified only as unnecessary surgery.

It has not yet been proved, either, that immediate operation is as safe an affair as its advocates would have us believe. In the hands of the surgeon of exceptional ability the claim is certainly justified. Victor Bonney lost one patient in twenty years, DuBose's mortality is one in four-hundred-nineteen cases, but in general practice the results are very different. I recently had occasion to study six hundred cases of salpingitis, treated surgically, from the records of Charity Hospital and of Touro Infirmary, which comprised the work of fifty-seven different surgeons. The series included both cooled and uncooled cases, and the gross death rate was 3 per cent, or three times as high as the accepted risk for surgery of the tubes. The rate for the cooled cases was less than 1 per cent, while the rate for the uncooled cases was 4.2 per cent. Or, to express it differently, approximately 90 per cent of the mortality occurred in patients who had not been properly cooled. It is something more than coincidence, too, that three-quarters of the postoperative morbidity developed in patients who had not been allowed to recover completely from their original infection. The death rate, you will note, is not the only point to be considered.

These figures from a composite series are to my mind far more representative than are the brilliant individual showings of such men as DuBose and Bonney. They prove again that the mortality of the average surgeon or the average mortality of all surgeons is a far better index to the wisdom or unwisdom of a given course than are the records of individual experts. It cannot be too often emphasized that while the experienced and dexterous surgeon may violate with impunity all surgical principles, such temerity on the part of the average man can lead only to disaster. On the surface it does seem paradoxical to permit a debilitating disease to run its course as a means of fitting a patient to withstand a major surgical procedure, but the facts prove the case.

Looking at it from another aspect, let me point out that immediate operation seldom permits conservatism. Since the involvement of the pelvic organs is general, since localization has not yet occurred, since nature's protective mechanism has not yet been set in order, total extirpation of the pelvic organs is frequently necessary. To quote DuBose's own words, "Pelvic debridement should include at least the removal of the pyogenic membranes with the infected tubes, uterus and ovaries." There is no semblance of conservatism in any such wholesale resection as that. If a competent surgeon is in charge the woman will probably emerge with her life, but she may also emerge with her sexual existence irrevocably ruined. And the tragedy of that lies in the fact that salpingitis is essentially a disease of young women, that the great majority of all cases occur in the prime of functional life. The argument that the tubes thus removed are functionless is unwarranted; Holtz's report, for instance, in which 12 per cent of pregnancies is shown to have followed purely expectant treatment utterly disproves that claim.

Finally, the various types of conservative operation which are supposed to be possible when immediate surgery is done have by no means justified the plan. Splitting and drainage of the tube is advocated with enthusiasm by one surgeon, another pleads for plastic operations such as are done during the chronic stage, a third advocates partial salpingectomy. Aside from the fact that the latter operation is particularly to be condemned because it may pave the way for a future ectopic pregnancy, not a single one of these procedures, as we shall point out later, can show the results which follow carefully ordered conservative methods. As one shrewd observer puts it, if pregnancy does not follow the old method of delayed operation, it is yet to be proved that it follows the revived method of immediate operation. And even granting the argument that a woman who has been treated expectantly and whose tubes are sealed obviously cannot bear children, even granting that argument, I would point out that that woman is no more absolutely sterile than is she whose tubes have been removed at laparotomy for acute salpingitis.

To my mind the only argument in favor of early operation which has the slightest weight is the argument of expediency. Often in private practice, more often on public hospital services, we are called upon to treat patients who cannot rest indefinitely, who cannot, for social or economic reasons, run the risk of a recurrence of their original condition. But even here there is no excuse for surgery until all the dicta of the delayed operation have been observed, absolute subsidence of the acute attack, resolution of the exudate, and a consistently normal temperature for at least two weeks in spite of repeated bimanual examinations, which, by the way, offer a better index of the patient's condition than any amount of laboratory work. It need

scarcely be pointed out that a woman who cannot stand the slight trauma of a bimanual examination without a febrile reaction is clearly unfitted to withstand the greater trauma of a laparotomy with its inevitable intraabdominal insults.

But when, you will ask, should operation be done? When is it finally justified? How long should one delay? I admit that once the patient has recovered from her acute attack the temptation is strong to operate in the interval, but even then the wise surgeon is the one who continues to wait. For one thing, only time can tell whether the first attack will not also be the last. This is frequently the case when the infection is of gonorrheal origin, and in nonspecific infections, as we have already pointed out, the longevity of the bacteria is an unknown quantity, so that the patient's safety is really best assured by an indefinite delay. A safe rule in all instances is to wait until the infection is thoroughly cooled and then to continue to wait. Even if the patient is not cured by this method, at least nothing is lost, for if the attacks continue to recur, if the symptoms continue unabated, if the patient's general health seems likely to be affected, operation can be done quite as safely later.

Moreover, the patient herself should have some voice in the matter, for she is the best judge of her own condition. If my patients consider themselves well, if they are able to resume their normal habit of life and to do their daily work with only brief periods of disability, I am quite willing to agree with them that they are well, even though the pelvic findings may not be entirely to my liking. It is possible, too, given the choice, that the patient may prefer to retain her organs, damaged though they be, on the chance of an ultimate clinical and functional cure. As Chipman well puts it, "Half a loaf, and a painful loaf at that, is better than no bread." A woman's sexual organs are the basis on which her whole life is founded, and her sexual sanctity, to express it as strongly as I can, should be violated only in the face of an urgent need, which a single attack of salpingitis rarely constitutes.

The wisdom of this plan has been repeatedly proved. In more than a thousand cases of salpingitis treated by purely expectant methods Holtz secured 82 per cent of clinical and 12 per cent of functional cures, and had only 2 per cent of absolute failures. Since 1921 in the clinic of Arthur Curtis of Chicago the plan has been to refrain entirely from operation for gonorrheal salpingitis on the principle I have already outlined, that recurrent attacks are fresh infections rather than fresh outbreaks of an original infection. The patients are isolated from their infected consorts, even douches are prohibited, and the treatment is entirely expectant. Not only have the clinical cures been brilliant, but the number of functional cures has been surprisingly large, and it may well be that another generation in medi-

cine will see surgery in such cases entirely eliminated and expectant treatment the routine plan.

It might be well to outline briefly the method by which these cases are handled. The cardinal principle is rest in bed, absolute rest, not for a few days but for many days, indeed for many weeks, until the temperature has been persistently normal for a minimum of two weeks in spite of repeated vaginal examinations. During the acute attack, pain is relieved by ice caps and local applications as indicated, with opiates used sparingly when necessary. The bowels are regulated by mild cathartics and gently given enemas; drastic cathartics have no place in the management of a pathology which can be excited to fresh outbursts merely by intestinal peristalsis. Fluids are forced by proctoclysis, by hypodermoclysis, even by infusion, and transfusion is resorted to in extremely debilitated and toxic patients. Douches are not routine but if they add to the patient's comfort and are cautiously given I do not believe them harmful. Surgery is limited to the opening of localized pus collections pointing in the culdesac or above Poupart's ligament. There is nothing subtle, nothing complicated about this treatment, and I sometimes wonder if its extreme simplicity, its total lack of action, is not the reason why more gynecologists are not willing to follow it absolutely.

When surgery is inevitable, its extent should be based not only upon the pathology present but upon the age and social condition of the patient and, to a certain extent, upon her own desires; if a woman is so situated that she can take the admittedly dubious chance of a functional cure which conservative surgery offers in specific infection, she has certainly the right to take that chance, provided she takes it with a full knowledge of the facts.

Speaking categorically, when the process is tuberculous or specific, bilateral salpingectomy is the wiser procedure; otherwise, unilateral removal of the affected tube will suffice, or sometimes the mere release of adhesions. Hysterectomy should not be done routinely, but only if the uterus is directly implicated in the infectious process, if it is myomatous or otherwise diseased, or if it is so denuded during operation that a useless organ would be left. That is, it should be removed on intrinsic indications and not because extrinsic disease happens to be present.

The same plan should be followed with the ovaries. I am aware that their conservation under such circumstances is still a matter of debate, but personally I believe that every effort should be made to save ovarian tissue. Naturally they must be removed if they are directly implicated in the infectious process, if they are riddled with cysts, or if the circulation cannot be preserved intact. Usually, however, they are not inherently diseased, they have simply been in bad company, and even if the other genital organs must be removed, their

conservation is still warranted. We have no present evidence that the ovaries cease entirely to function at any portion of a woman's life, and if they do nothing more than supply internal secretion to the host they still should be preserved when possible. If extensive resection is necessary, I might add, transplantation is a preferable procedure; its field is limited, but I have more than once seen it avert the trying symptoms of a precipitate menopause in young women.

In this brief paper it has naturally been impossible to handle all phases of the subject, but I hope I have succeeded in making at least one point clear, that salpingitis is an infectious disease in which autosterilization will occur under expectant treatment in the great majority of cases and in which a spontaneous cure, at least clinically, is possible in a very fair majority. There is no indication, therefore, for immediate surgery in any case and often there is no indication for delayed surgery either. The patient has a right to her chance to preserve her sexual apparatus and it is unfair to deprive her of it. If surgery must eventually be done, if after a reasonable trial it is clear that a complete cure cannot be hoped for, then let the operation be radical enough actually to cure the disease, being sure, however, that this ruthlessness is not extended to organs which are not intrinsically involved in the infectious process. In tubal disease almost more than in any pathology of the female pelvis, the sanest surgeon, the wisest gynecologist is he who refrains longest from the practice of his art, but who, when he is obliged to exercise it, tempers his conservatism with sufficient radicalism to ensure for his patient a permanent cure.

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Seckinger, D. L., and Snyder, F. F.: Cyclic Changes in the Spontaneous Contractions of the Human Fallopian Tube. Bulletin Johns Hopkins Hospital, 1926, xxxix, 371.

The cyclic changes in the activity of the muscular wall of the tube closely parallel chronologically the histologic changes occurring in the endometrium and tubal mucosa during the reproductive cycle as follows: During the mid- and late-interval stage, there are rapid contractions showing a marked variation in amplitude. During the premenstrual and menstrual phase, slow contractions of uniform amplitude are found. During pregnancy tubal contractions remain slow and of uniform amplitude.

Comparison with other mammals suggests that in the human the increased activity of the tubal wall during the mid- and late-interval stage is probably coincident with the passing of the ovum through the tube.

No change in the number or activity of the cilia lining the tube was noted at any phase of the reproductive cycle. C. O. Maland.

THE DIAGNOSIS OF FETAL DEFORMITIES IN UTERO*

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THE purpose of this paper is to present certain facts observed in the study of a series of deformed fetuses in utero and to formulate, if possible, a syndrome that will be of use in the diagnosis of these cases.

The diagnosis of a deformed fetus in utero is not new, but it is only in recent years with the development of the x-ray that the clinical impression of the probability of a fetal deformity in a given case could be absolutely confirmed. As early as 1883 Laulaigne[1] described a syndrome based on four rules Pinard had laid down which included: permanent exaggerated tension of the uterus; difficulty in finding the fetal poles; weak heart tones; easy and exaggerated ballottement.

Negri[2] in 1899 reported two cases and Viana[3] in 1905 two more cases in one of which he was able to produce the convulsive movements of the limbs and presenting part by palpation in spite of the attendant hydramnios. Gilio[4] in 1896 stressed the syphilitic history, the abnormal movements, a transient albuminuria, vaginal examination during labor, weak and uncertain heart tones which he ascribes to poor cardiac innervation. The tentative diagnosis made by these writers was confirmed after the birth of anencephalic monsters. By means of our modern methods the diagnosis may be confirmed before the birth of the fetus. Furthermore, other deformities in addition to anencephalic monsters have been diagnosed in utero in recent years.

Accurate diagnosis is the more important since on it the decision of the obstetrician must be based as to what line of treatment shall be pursued, and its probable effect on two patients instead of one. In certain instances it may seem wise to increase the risk for one in order to reduce the danger for the other. A correct estimate of the condition of both patients at the time the decision has to be made, therefore, is of paramount importance.

The decision as far as the mother is concerned is based on a careful physical examination together with accurate special tests of the excreta, blood and the application of specially devised instruments such as the ophthalmoscope, cystoscope, and sphygmomanometer, x-ray, etc. By these means and others, especially if the findings can be supplemented by careful clinical observation for a period of a few days or weeks, a fairly satisfactory estimate of the condition of the mother can be determined.

*Read before the Chicago Gynecological Society, Jan. 20, 1928.

Our opportunity to judge of the condition of the fetus, on the other hand is far less favorable. The ordinary means of palpation, percussion and auscultation are only applicable to a limited degree even in the most favorable subjects. In patients with abnormally fat abdominal walls, an early pregnancy, irritable uterus, or hydramnios, these methods may be quite useless. The application of special function tests is obviously out of the question.

One of the most valuable of the diagnostic aids in this connection is the x-ray. The use of the x-ray in the diagnosis of obstetric conditions was somewhat limited in the early years of its development and before the use of the Bucky diaphragm by the fact that clear pictures were difficult to obtain owing to the thickness of the abdominal and uterine walls, and the liquor amnii which interferes with the proper penetration of the rays. Formerly it was thought that care was necessary to avoid injuring the growing embryo by the x-ray. This danger is, however, theoretical rather than real, as pointed out by Case[5] because of the short exposures necessary with the present technic.

There are a group of cases which are particularly difficult to diagnose by ordinary clinical methods and which are usually not diagnosed until late in labor or after the birth of the baby. These are the various types of fetal deformities which are relatively frequently associated with an hydramnios which obscures the physical findings.

It is particularly important to make a diagnosis previous to delivery in these cases for several reasons. In the first place the shock to the mother and family can be made less if a responsible member can be acquainted with the facts in the case before the birth of the child. Secondly, the discomfort of the patient due to the continuation of pregnancy in the presence of hydramnios may be relieved by inducing labor. Thirdly, the confidence of the patient in the skill of the medical attendant is increased by the proof of his diagnostic ability. Fourthly, if for any reason cesarean section or other operative intervention should be indicated in a given case, the presence of the fetal deformities should be given due consideration. Fifthly, the danger of postpartum hemorrhage due to overdistention of the uterus by the hydramnios may be minimized by induction of labor as soon as the condition is diagnosed and proper preparations may be made to treat this complication if it occurs.

Our interest was first aroused in the subject of x-ray diagnosis of abnormal fetal conditions by the diagnosis which we made and reported in 1917 of a fetus in opisthotonus position. All attempts to correct the position failed before labor set in. Following the rupture of the membranes at the end of the first stage, the fetus died before a version and extraction could be done.

The earliest reference we are able to find in use of the x-ray in the diagnoses of intrauterine pregnancy is by Albert,[7] 1899 at a meeting of the German Society

of Gynecologists. He showed a number of roentgenograms in which the fetal heads and some of the bones could be clearly seen.

H. Freund[8] in 1905 stated that the fetal skeleton was not visible until the second half of pregnancy, but he believed in the possibility of recognizing deformed fetuses, although he reports none.

Von Jaksch[9] in 1911 stated that he had repeatedly succeeded in visualizing the gravid uterus from the second month. He used metal filters and rather hard tubes, the time of exposure being from twelve to fifteen seconds. He also said the roentgen exposures were harmless as far as the pregnancy was concerned.

Lars Edling[10] in 1912 stated that the diagnosis in the early stages of pregnancy depended on the state of ossification, which was usually sufficiently complete during the third month. In most cases only parts of the skeleton could be seen. He also reported a case where the roentgen examination failed to diagnose an existing pregnancy. He believed hydrocephalus and certain double monstrosities could be roentgenologically recognized, although he did not examine any such cases. He had a successful roentgen of twins, except that it proved to be triplets which he failed to notice.

Spangler[11] in 1924 reported two anencephalic monsters, the first of these delivered February 6, 1921. The diagnosis was made because a marked hydramnios interfered with the palpation of the presenting part. The x-ray revealed "no fetal cranial bones, vertebrae very poorly developed, length of spinal column less than normal, with the bones of the face close to the thorax."

The second case developed a severe toxemia of pregnancy, a blood pressure of one hundred forty systolic, one hundred ten diastolic. The uterus at eight months was not so large as it should have been and x-ray taken because of this discrepancy revealed anencephaly with marked shortening of the vertebral column. This baby was stillborn and delivered January 20, 1923.

Campbell and Willits[12] in the same year reported an anencephalic monster which was diagnosed in 1923. This diagnosis was made by palpating a soft mass surrounded by a hard oval ring with the finger introduced through the cervix of the uterus.

Daub[13] in 1925 reported an anencephalic monster born January 3, 1924. The patient had a marked hydramnios and because the fetus could not be palpated she was referred to x-ray. The latter disclosed a well developed anencephalic monster and a defect in the upper portion of the spinal column which he regarded as a spina bifida. In August of the same year he examined another patient with a moderate hydramnios which revealed no malformation except a lack of development of the skull bones which gave the impression of an anencephalic fetus.

Daub[13] in 1926 reported a hydrocephalus which was examined with x-ray about the seventh month because of breech presentation. The skull appeared to be normal at this time. During the ninth month a large mass was felt in the region of the fetal head and by means of a second x-ray a definite diagnosis of hydrocephalus was made. This is the first diagnosis of hydrocephalus in utero that we have been able to find.

Rudolph[14] delivered a case in May 16, 1925 of a thirty-two day postmature anencephalic monster weighing nine and a half pounds. Great difficulty was experienced in bringing on labor pains in this case. A marked hydramnios interfered with the abdominal examination, rectal and vaginal examinations failed to make a definite diagnosis of presentation and position and aroused the suspicion of the possibility of a deformity of the fetus. An x-ray revealed the anencephalic nature of the deformity.

Case in 1926 reported three additional cases. The first case was referred for x-ray examination because of marked hydramnios interfering with the diagnosis of the position of the fetus. The cranial vault was found to be absent. The

second case also presented herself with a marked hydramnios which interfered with palpatory findings. The x-ray pictures revealed an anencephalic monster. The third case showed the uterus enlarged to the size of a full-term pregnancy when according to her history she was only about seven months pregnant. The head could not be palpated and the fetal heart tones could not be heard. A vaginal examination disclosed slight dilatation of the cervix through which with one finger it was possible to feel what was thought to be the rough edges of a fetal abnormality. An x-ray examination showed cephalic presentation and an anencephalic monster.

Lascano[15] in 1923 reported a case of anencephalus diagnosed in utero by means of palpation through the cervix alone. Thoms[16] and Ballard[17] each report a similiar case.

Our attention was first called to the possibility of diagnosing monstrosities in utero by a report of Case of Battle Creek, Michigan, before this Society in 1917. He took an x-ray picture of an anencephalic monster in utero after abdominal and vaginal examinations had failed to determine the diagnosis and aroused the suspicion that the head was abnormal. The x-ray plate demonstrated the deficiency in the cranial vault clearly. No heart tones were heard and a second picture a month later revealed the same findings without evident growth of the fetus. Labor was induced and a 27 centimeter anencephalic monster was delivered.

We became interested in the subject and in 1921 observed our first case. Following this we observed three other anencephalic monstrosities and during the last year have observed a very interesting double headed monster, a spina bifida, and two hydrocephalic monsters.

In those cases showing an anencephalic monster a greater or less degree of hydramnios is usually present. When this is extreme no accurate palpatory findings can be noted. Even when the hydramnios is not great, or the membranes have ruptured, difficulty will be encountered in definitely locating the fetal head, since the normal hard round smooth object is absent, and the difficulty is increased if the head is in the fundus of the uterus.

On executing the fourth maneuver of Leopold in cephalic presentations no cephalic prominence will be noted. We noted lively movements of the fetus in our cases but did not elicit the abnormal spasmodic movements described by Pinard, Laulaigne, and others. We did not know of this sign when studying our cases.

On vaginal examination it may be difficult to determine whether the head or breech is presenting until after the partial dilatation of the cervix and rupture of the membranes. The soft meningocele may exactly simulate the breech. Frequently the diagnosis is not made until the head is on the perineum. The soft meningocele surrounded by the bony edge of the defective cranial vault has been said to be characteristic. In one of our patients the face presentation did not permit of this observation.

Another vaginal finding which is said to be characteristic and which we have been able to confirm has been the elongated form of the bag of waters protruding through the cervix after 4 or 5 centimeter dilatation.

When no x-ray is available and the diagnosis of anencephalic monsters is probable from the abdominal examination, it is possible to confirm the diagnosis by placing the patient under general anesthesia and introducing a finger or, after complete dilatation of the cervix and rupture of the membranes, the whole hand into the uterus. The deformity of the head can thus be easily appreciated. The heart tones are frequently found to be unduly rapid or unduly slow with and following labor pains before the head is engaged. Occasionally irregularity of rate is noted before labor starts. The probable explanation of this is that the medulla, unprotected by the bones of the cranial vault, is irritated by the increased intrauterine pressure resulting in stimulation of the cardiac centers. The point of maximum intensity of the fetal heart tones was noted to be unusually low in the abdomen as compared with those of the normal fetus with the same degree of engagement of the head as determined by rectal or vaginal examination. Ths is due to the lack of the cranial vault and the shortness of the neck. Rates varying from forty to one hundred and seventy and higher have been observed. There may be considerable difficulty in hearing and counting the heart tones due to the muffling by the liquor amnii.

The x-ray picture will usually show the deformity after the seventh month of gestation, and although the outline of the fetus and the skull may be somewhat obscured by the hydramnios it should show the defect in the cranial bones. The contrast with the rounded vault of the normal head is easily appreciated.

A study of the family history was not of value in any of these cases, there having been no similar monstrosities born in these families as far as the patients knew. This is somewhat against the general impression that monstrosities tend to occur in families, and to repeat in the same patient.

The treatment of this condition is the termination of the pregnancy in the most conservative manner as soon as the diagnosis is made. Induction of labor by Watson's method may be tried and failing the procedure may be repeated after a rest of three or four days. If it again fails a bag induction may be advised. This is particularly desirable if the hydramnios is severe enough to cause pressure symptoms. The rupture of the membranes before inserting the bag and draining off a large part of the liquor, may assist in developing strong contractions. If any unusual obstruction is offered by the bony pelvis, craniotomy or embryotomy should be undertaken as soon as normal parturition is interfered with. If such a baby is born alive as

they not infrequently are, the chance of its surviving for more than a few days is very remote. It is best to keep it separated from the mother, and to withhold the diagnosis from her when feasible, simply telling her that the baby did not survive the labor. The information, of course, should be given to the husband or some responsible member of the family as soon as the diagnosis is made and confirmed. The baby should be kept warm and sterile dressings over the meningocele. In spite of such precautions a meningitis will almost surely develop if the baby does not die of inanition.

Whenever in a given case for various indications such as contracted pelvis, or abnormalities of the pelvic soft parts, a cesarean section may be considered the choice of operation for delivery, if there is any suspicion of fetal abnormalities, careful x-ray examination should be made before electing this operation. It is not justifiable to jeopardize the mother for such a baby.

The following case histories are presented:

CASE 1.—F. L., entered the obstetric department of the State University of Iowa on December 13, 1921, young, well nourished, white, aged nineteen, a school teacher and not married. Menses began at twelve years, were regular every twenty-eight days, lasting five to seven days, flowed an average amount with occasional pain. She denied previous pregnancies. Her last period was April, 1921. She admitted a single intercourse the last of March, 1921.

She had had measles, chicken pox, and whooping cough, scarlet fever in 1914, influenza in 1918, and smallpox vaccination in 1915. She had had a sore throat three weeks before admission and her hands and ankles had been somewhat swollen for three weeks. The digestive, nervous, and genitourinary systems were negative except as previously noted. There was no family history of carcinoma, Bright's disease, diabetes, or tuberculosis. Her mother had no abnormalities in her obstetric history as far as the patient knew. Heart and lungs normal. No glandular dystrophy. Breasts normal in contour and secretion. Slight edema of the lower extremities. The abdomen was greatly distended and tense. Fetal heart tones not heard and fetal parts not clearly outlined. Fetal movements, however, could be heard and felt and seemed to be unusually active. Rectal examination revealed a small part presenting and the cervix almost completely effaced but not dilated. The pelvic measurements normal. Vaginal and urethral smears were negative for the gonococci. The Wassermann test was negative. Urine was amber color, specific gravity 1018, no sugar, no albumin, many pus cells. Blood pressure varied from 150 to 180.

On December 18, the patient complained of irregular pains during the night, and at eleven A.M. discharged from the vagina what seemed to be amniotic fluid. Rectal examination revealed no dilatation, pains every ten minutes but weak. Fetal heart tones heard but not counted. Labor continued about the same all day, and practically stopped by midnight.

January 2, she began again to have pains at 11 A.M. and was taken to the delivery room with two fingers' dilatation. Fetal movements were easily stimulated and visible in the lower left and the upper right quadrants. Fetal heart 144 and irregular. X-ray revealed an anencephalic monster, cephalic presentation. Membranes ruptured at 5:40 P.M. and about three gallons of amniotic fluid were expelled. Before rupture the elongated shape of the bag of waters was noted.

Spontaneous delivery occurred at 6:40 P.M. of an anencephalic monster weighing four pounds and eight ounces. The heart beat for five minutes but the baby did not breathe. Estimated blood loss was 200 c.c. The placenta contained numerous small infarcts and there was a marginal insertion of the umbilical cord. The cord itself showed numerous twists. The puerperium was uneventful except for a mild thrombophlebitis of the left leg.

CASE 2.—G. S., primipara, single, aged nineteen years. Entered the clinic August 31, 1923. Nothing of importance in the family history. She had had diphtheria, and infantile paralysis with a deformity of the right foot. The tonsils and adenoids were removed at seventeen. Menses began at fifteen years, regular every twenty-eight days, lasted five days, moderate, no pains. The father of the baby weighed one hundred and fifty pounds, twenty years of age, white, laborer, and nothing was known as to whether he had venereal disease or tuberculosis. She thought her last period had been in November, 1922, and that she had felt quickening March 17, 1923.

General examination was negative except for the deformity of the right foot. Presenting part was thought to be the breech, sacrum right anterior, and it was thought it had advanced to about seven and one-half months. The fetal heart tones were clear, 132. Pelvic measurements were slightly smaller than normal. It was difficult to palpate the head because of mild hydramnios present. X-ray taken August 8, 1923 showed an anencephalic monster. Blood Wassermann was negative to both alcoholic and cholesterinized antigens. The urine was quite clear, and blood pressure ranged from 130 to 166.

She went into labor September 24, at six o'clock in the evening. Ovoid was longitudinal, head over the inlet, breech in the fundus, back to the left, shoulder low over the pubis. The baby was estimated to weigh six pounds. Fetal heart tones ranged from 138 to 144 throughout the first stage. The second stage began at one o'clock in the morning, and at two twenty the fetal heart tones fell from 138 to 40 and most of the time were around 100. The pains were strong. The birth was spontaneous, cephalic. The third stage was rapid. The baby was an anencephalic monster, which lived eight hours and ten minutes.

CASE 3.—N. K., primipara, married, twenty-five years of age. No history of monstrosities in the family. No chronic diseases in the family. She had the ordinary diseases of childhood. Was operated on for appendicitis on May 16, 1923, in the early part of this pregnancy. Otherwise in good health. Menses began at thirteen, regular every twenty-eight days, lasted two or three days, scant and always painful. No miscarriages. Father of the baby was five feet four inches tall, weighed one hundred and thirty-five pounds, forty years of age, white, laborer, denied venereal disease or tuberculosis.

The first day of the last period was March 12. She felt quickening July 1. Blood pressure was 110 systolic, 65 diastolic. General examination was negative. Fundus was halfway between the umbilicus and the xyphoid on November 17, 1923. The presenting part could not be made out but it was thought to be a head. Fetal heart in the left lower quadrant, rate 130. Measurements were normal. Blood Wassermann negative to alcoholic and cholesterinized antigens. X-ray was not taken in this case since the diagnosis was not suspected. There was no hydramnios present.

She went into labor December 6, at five-thirty P.M. Ovoid longitudinal, inlet moderate, breech in fundus, back to the right. Fetal heart irregular, varying in the first stage from 164 to 120, sometimes clearly audible. Eight rectal examinations were made between five P.M. December 6, and eight forty A.M. December 7. Presentation was at first thought to be breech, then was changed to a brow, and then to a face. During the second stage, which began at five P.M. on December 7,

the heart tones varied from 148 to 69, and were poor in quality. Anencephalic monster was stillborn after one hour and forty minutes in the second stage. The placenta and membranes were apparently normal.

CASE 4.—G. S., primipara, fifteen years of age, single, white, entered the clinic August 15, 1925. Wassermann was negative. Family history for twins or monstrosities negative. The patient had had measles, mumps, chicken pox, influenza and malaria, tonsils normal to date. Menstruated at eleven and one-half years of age, every twenty-eight days, lasting three to four days, moderate in amount, no pain. The father of the baby was her stepbrother, healthy, five feet tall, weighed one hundred eighty pounds, a high school student.

There were no toxic symptoms and her heart, lungs, teeth, nervous system were negative. There was slight edema. She was stocky, five feet tall, weighed one hundred and eighteen pounds, the breasts showed colostrum, and the position of the baby was L.O.A. The size of the abdomen was slightly more than eight months, and the fetal heart tones were 140. Pelvic measurements normal.

Labor began September 18, 1925 at eight A.M. Blood pressure was 115/75. Ovoid longitudinal, head over the inlet, but it was a questionable diagnosis. X-ray taken August 18, 1925 showed an absence of the fetal head. The baby weighed 2170 grams, and was 45 cm. in length. Heart tones irregular, varied from 100 to 160 during the first stage, and went as low as fifty-six during the second stage. The baby was born alive, brow right anterior and was very weak and listless. The placenta was small; 100 c.c. of blood lost. No hydramnios was noted, and the fetal heart tones had only one sound. The heart tones before labor were found in the midline and most clearly just above the symphysis. The baby lived three days.

CASE 5.—A. S., entered the hospital March 7, 1925 in the second stage of labor with the bag of waters ruptured, and a foot presenting. The patient was seventeen years of age, primipara, with a negative family history for twins or other monstrosities. Patient had had all of the ordinary diseases of childhood, scarlet fever, and influenza in 1918, and had frequent attacks of tonsillitis and sore throat. No miscarriages. No history was obtainable about the father of the baby. She had slight edema and some dizziness. Weighed one hundred and forty-six pounds.

Pains began March 7, 1925 at ten A.M. and the bag of waters ruptured at one fifteen P.M. She entered the clinic at two-thirty with the fetal foot protruding, no heart tones were heard. Pains were strong, and the fetus was born dead at two fifty-five. Placenta was complete with an eccentrically implanted cord. 400 c.c. of blood was lost.

CASE 6.—N. S., white American female, aged twenty, married, para i. Felt quickening in March. At term September 30, 1927. Her period in December lasted only one and a half days, instead of the usual four or five days, therefore, her last regular period was in November. She had the usual vomiting in January and February. She had marked edema one week before entering the hospital. Had slight dizziness and vomiting two weeks before admission. Also some gastric pain.

Menses began at fifteen, irregular, lasted for five days, small in amount and painful. Had influenza in 1918, no surgical operations. Mother had carcinoma of the stomach, father died of tuberculosis, two sisters and four brothers alive and well. Patient is a twin, also her cousin has twins. Father of the baby is five feet seven inches tall, weighs one hundred and thirty-seven pounds, twenty-two years of age, laborer, denies venereal diseases.

Patient entered the Out-Patient Department April 4, 1927, at which time the diagnosis of pregnancy, duration twenty-three weeks, cephalic presentation was made

and no heart tones were heard. A month later the heart tones were heard, rate 140, and the diagnosis of cephalic presentation L.O.A. was made. On July twenty-third twins presenting by the breech was diagnosed, and she was sent to x-ray for confirmation. The x-ray picture was diagnosed twin pregnancy about six or seven months presenting by the breech. Two heads were found in the right iliac fossa and the spines indefinite and in close approximation to each other. Monstrosity was suspected and a second x-ray was taken a week later and a dicephalic monster diagnosed.

On September 7, 1927 she had considerable bleeding and was ordered into the hospital. Heart and lungs normal. Fetal heart varied from 124 to 156. On entering the hospital she was found to have a breech presentation, slightly movable, fetal heart 128. There was no cervical dilatation, the os was thick and the presenting part not engaged. The patient was having some pain in the lower abdomen and had lost about two to three ounces of blood. On September 8 she lost about another ounce and continued to ooze thereafter. Fetal heart irregular, from 136 to 160. A diagnosis of placenta previa was made and because she was a primipara and also because of the difficulty anticipated in the delivery of the double head in the presence of a placenta previa and a preeclamptic toxemia, a cesarean section was elected. The blood pressure during her stay in the hospital had risen from 98 to 194 systolic.

Classic cesarean section done September 12, 1927, indications were a slightly contracted pelvis, a marginal or possibly a lateral placenta previa in a primipara, together with a double headed monster and a mild preeclamptic toxemia. It was done in the usual way, slight increased difficulty was experienced removing the fetus from the uterus especially with the shoulders and heads. The placenta was delivered following the birth of the baby, was normal in appearance, one amnion and chorion. It seemed to be implanted in the lower uterine segment but whether marginal or lateral type of placenta previa could not be determined. The baby was a dicephalic monster.

A dissection of the specimen revealed a duplication of the structures of the head and neck, together with two spinal columns. There was only one heart, and four lungs in four plural cavities. The abdominal viscera were normal in number and size as were the extremities. A detailed description of the specimen will be given in another report. The length of the fetus was forty-one centimeters and it weighed 2690 grams.

CASE 7.—White, American, aged nineteen. She was sent in from the Out-Patient Dispensary because of high blood pressure January 22, 1927. Her last menstrual period was April thirteenth, and she had no special toxic symptoms. Her menstrual history began at twelve, moderate every twenty-eight days, flowed five days, few cramps. She had had no previous pregnancies. She had measles, mumps, chicken pox, and influenza. No history of twins or monstrosities in the family. Her husband was twenty-five years of age, six feet tall, weighed one hundred and eighty-five pounds, laborer.

Physical examination showed an obese, white female, weighing two hundred and fifty pounds. General physical examination was negative. Abdominal examination revealed thick walls, obese, no scars or hernia. The fundus of the uterus was two fingers' below the xyphoid, irritable, and there was more than the usual amount of liquor amnii. Because of the softness of the head, the thickness of the abdominal wall, and the mild hydramnios a breech presentation was suspected. The x-ray examination on January twenty-fourth revealed the unusual size of the head together with the defect in the lumbar spine. Abdominal palpation was seriously handicapped by the stoutness of the patient. The unusual size of the head was not easy to detect

by palpation, even after the x-ray had made the diagnosis. The position was right occiput-anterior, and the head was movable. The pelvic measurements were: interspinous 31.5, intercristal 36, bitrochanteric 47, Baudelocque 27. The blood pressure was 148/104. The phenolsulphonephthalein test was done and the dye appeared in twenty-two minutes, forty-two per cent was recovered in the first hour and eight per cent the second, or fifty per cent for the total for two hours. The Wassermann and Kahn tests were negative. The blood chemistry was normal for alterations of the sugar, nonprotein nitrogen, uric acid, urea, and creatinine. Urine showed no albumin, no casts, sugar was positive.

Watson's method of inducing labor was tried January 25, 1927 but failed, and on the twenty-seventh it was tried again and failed. On the twenty-ninth the patient went into weak labor with a blood pressure of 172/120, position R. O. A. Fetal heart 140. On the thirtieth, the pressure was 160/110, position R. O. A. heart tones could not be well heard, and the pains were weak and inefficient. On the thirty-first the pressure was 194/124, pains coming every two minutes, position R. O. A. the head engaged. On the thirty-first at one-thirty A.M. the pains became more severe, every two minutes, head engaged, heart tones 136. At seven A.M. the blood pressure was 160/120, pains every minute, R. O. A., head engaged, fetal heart tones 150, irregular. The baby was born spontaneously, male hydrocephalic infant, showing spina bifida, weighed 3900 grams, fifty-four centimeters long and could not be resuscitated.

CASE 8.—Patient twenty-six years of age, para iii, colored. She was admitted on February 22, 1927 at twelve A.M. with blood pressure 140/112. Contractions fair, pains every five minutes, fetal heart 160. Rectal examination showed the cervix not dilated, membranes intact, presentation and position not made out. The presenting part was not engaged. The pains were weak and inefficient, persisted for forty-eight hours. Fetal heart 160, regular. An x-ray was taken on the twenty-fourth, the report, a normal fetus. Slight labor pains on the night of the twenty-fifth and twenty-sixth. Fetal heart tones dropped to 140. There were no labor pains from the twenty-seventh to the thirty-first, when interrupted pains began.

On April 1, 1927 about 1 P.M. because the pains were dying down and had been weak and inefficient, the membranes were ruptured and fourteen pints of liquor amnii drained off. Heart sounds 120 after the rupture. In order to let out all of the liquor amnii the resident pushed up on the head and this produced a transverse presentation which turned spontaneously to a breech. The heart tones became irregular about four P.M. varying from 76 to 116. An x-ray picture taken at this time revealed the breech presentation and the head was thought to be normal. Clinically, however, the head seemed to be larger than normal and softer. Because of the x-ray report and the bad heart tones we felt a rapid delivery should be undertaken to give the baby the benefit of the doubt. The cervix was dilated by the Harris method and the fetus was extracted until the head engaged in the inlet.

Despite the application of considerable traction the head would not come through the inlet. Examination clearly showed the disproportion between the head and the inlet and the cardiac action had ceased. Therefore, a craniotomy was done on the after-coming head. The baby weighed five pounds six and one-half ounces without the brain. The placenta measured nine by six inches, the cord was eccentrically implanted, twelve inches long, and the membranes were ruptured laterally. The placenta was intact containing occasional white infarcts. The sutures and fontanelles were wide and unmistakable evidence of hydrocephalus was found.

In addition to these cases we have delivered two fetuses in the clinic with spina bifida in which the deformity was entirely unsus-

pected before delivery. In Case 10 the presence of a marked hydramnios should have prompted the taking of an x-ray picture but this was not done.

CASE 9.—Patient thirty-one years, colored, para iv. She was referred from the Chicago Lying-in Dispensary on February 8, 1927 because of cardiac and venereal disease. A diagnosis of nephritic toxemia was made. She entered the clinic February 8 and was estimated to be due about the middle of February. There was a history for the last six months of cough, swelling of the ankles and inability to lie down. She lost her first and second babies in 1921 and 1922 and was told she had kidney trouble. Her last baby was born alive, weighed five pounds ten ounces. Menses began at twelve, regular twenty-eight days, and flow lasted four days, moderate in amount, some cramps the first two days. She denied gonorrhea and syphilis. The past medical history was positive for measles, mumps, whooping cough, and chicken pox, and she had frequent attacks of sore throat and rheumatism during the previous year which lasted three or four days. She denied scarlet fever and had had no surgical operations. The general examination was negative as far as the head, neck, and glands were concerned. The lungs showed pulmonary edema, patient's abdomen was enlarged, the heart was badly decompensated and the pulse 108. The fundus of the uterus was below the xyphoid, and the uterus was not irritable. The fetus was in L. O. A. position. Fetal heart heard in the lower left quadrant rate 144. There was nothing in the findings or history of this case to make one suspect an abnormality of the fetus. Blood pressure was 172/130 and the phenolsulphonephthalein test was forty-five per cent in two hours.

She was given digitalis and between the eleventh and seventeenth, she improved steadily and on the eighteenth a Voorhees bag was inserted which was expelled in six hours, and on April 29 a macerated fetus was extracted which showed a small spina bifida in the lower lumbar region. It weighed four pounds and one ounce and was forty-five centimeters long.

CASE 10.—White, American, para i, illegitimately pregnant, was estimated to be due May 21, 1927. There had been no abnormal pregnancies in her family history and her menstrual history was negative. She had tonsillitis every winter until eleven years of age and had a tonsillectomy in 1921. She had had measles, mumps, and scarlet fever as a child, denied venereal disease. The father of the baby was five feet nine inches tall, weighed one hundred seventy pounds, a mechanic, twenty-one years of age, had no tuberculosis.

The physical examination was essentially negative. The first examination showed a marked hydramnios and the fetal parts could not be palpated easily. The fetal heart tones were 140 and heard in lower left quadrant. There was no suspicion from these findings that there was anything abnormal about the case, therefore, an x-ray was not taken. The patient went into labor November 17, 1927 and delivered a full time baby forty-nine centimeters long which had a spina bifida and a club foot.

With the exception of the hydramnios in Case 10 the symptoms in both cases of spina bifida were entirely negative.

The appearance and delivery of these monstrosities in our clinic where the interest in this subject has been considerably stimulated by the previously mentioned cases, demonstrates the difficulty of diagnosing this type of deformity unless a chance x-ray picture is made for some other indication.

From a study of the case histories in which the information regarding previous infection in these cases was noted it will be seen that syphilis as gauged by the Wassermann reaction was rarely present. This was diametrically opposed to the experience of Gilio. On the other hand we have noted a large number of acute infectious diseases in the cases that we have studied. Influenza, measles, mumps, pneumonia, smallpox, scarlet fever, and other serious systemic infections have occurred. The possibility at once suggests itself that there might be some etiologic connection. It is certainly conceivable that these serious infections might have some deleterious effect on the dormant egg cell in the ovary, and result in abnormal development after fertilization.

The associated lumbar spina bifida in one case, which as far as we know is the only lesion of this kind reported up to the present time, can also be clearly seen. The bones of the fetal skeleton are somewhat obscured by the associated hydramnios. One case of hydrocephalus of a less marked degree could not be accurately diagnosed even with two x-ray pictures. The deformity of spina bifida alone gives so few signs and symptoms that its presence is rarely suspected in utero.

CONCLUSIONS

From a clinical study of the foregoing cases it would seem that the following signs and symptoms when present in a given case are strongly suggestive of a deformed fetus in utero:

1. Hydramnios coming on usually about the seventh month and associated with permanent exaggerated uterine tension and easy ballottement is suggestive of fetal abnormality. This condition is not constant with fetal deformities.

2. Inability definitely to outline the fetal head suggests anencephalus while abnormal size or consistency indicates hydrocephalus.

3. Difficulty is experienced in differentiating between the fetal poles either by abdominal or vaginal palpation when the deformity is anencephalus.

4. In anencephalic monsters a soft meningocele surrounded by a bony ring may be felt on vaginal examination with a finger inside of cervix in cephalic presentations.

5. Fetal heart tones are heard faintly or not at all when the hydramnios is marked. They are usually normal or rapid during pregnancy, but during labor they are often slow and irregular or abnormally fast. With cephalic presentations, in anencephalic monsters they are frequently heard unusually low in the abdomen during labor, and the irregularity is most marked in these cases.

6. Abnormally active fetal movements, which may become convulsive if pressure is made on the head in cases of anencephalic monsters, may be seen and felt.

7. X-ray pictures which will clearly determine the deformity as early as the sixth month, in anencephalic, hydrocephalic or spina bifida fetuses, but a negative picture does not rule out the possibility of a deformity.

The above points may serve as a syndrome for the diagnosis of these monstrosities in utero. We feel if they are carefully observed that the birth of these monstrosities undiagnosed will rarely occur.

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(For discussion, see page 894.)

ARTIFICIAL PRODUCTION OF STERILITY

With Special Reference to Experimental Temporary Sterility Biologically Induced in the Female

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THE present-day method of defeating fertility in civilized communities is by the induction of abortion or the practice of contraception. That many pregnancies are prevented or terminated by artificial means is a well-recognized fact. Changing social conditions, by giving woman a definite status in the business world, have done much to discourage the natural function of childbearing. Many women who continue to work after marriage feel that their economic status will not allow them to resign their positions and therefore sacrifice or postpone motherhood. Another type of woman who frequently resorts to contraception or abortion, or both, is the mother of a large family who is weary of the obligations of rearing children and feels that she is entitled to a respite. Usually some one of the various methods of contraception is utilized; but, when this fails, abortion is generally induced.

The frequency with which abortions are performed is appalling. Professor V. S. Gruzdev,[1] of the University of Kazan, states that there is actually a pandemic of abortions spread all over the world, invad-

ing even the most remote rural districts. According to L. L. Okontchitz,[2] the percentage of abortions admitted to the Nadejdinsky Maternity Institute in 1903 was 7.5 per cent of all admissions; in 1912, it was 17 per cent; in 1923, 21 per cent. In 1926, 3,000, or 25 per cent, of the 12,000 admissions were for abortion.

From the data available in my files, I have compiled statistics in an endeavor to estimate the frequency with which women resort to abortion. The records of 13,800 women, 6,368 of whom were of functional age, were studied. Of these women, 1,974 gave history of 2,796 abortions, which in 2,730 cases were either admitted or assumed from the history to have been induced.

Aside from the moral aspect, the evil consequences of abortion to the patient herself are admitted. Death from perforation of the uterus, septic infection or uncontrollable hemorrhage is fairly common. Pelvic infections not proving fatal may result in years of semi-invalidism and also permanent sterility. The average woman is well aware of these dangers; but, when the infant is unwelcome, she is not deterred.

CONTRACEPTIVE METHODS UNSATISFACTORY

Birth control is a procedure which few mention but many practice. Especially is this true of the various means of contraception to which perhaps the majority of couples resort at some time or other during their married lives. The measures employed include coitus interruptus, condoms, douches, vaginal globules, pastes, sponges, vaginal and cervical occlusive pessaries, and even intrauterine injections. None of these methods of contraception is infallible. Some of them are uncertain; others, reliable but harmful in their effects on the nervous system because of the failure fully to consummate the sexual act; still others produce direct injury to the female sexual organs. All of them are decidedly inconvenient at times and do not permit of anything like normal sexual relations.

In view of the unsatisfactory status of contraceptive measures, and not as a means of furthering the Malthusian movement indiscriminately, we should strive to devise a safe method of inducing temporary sterility in the female where indicated for medical reasons only.

Under medical guidance, there could be no objection to the legitimate induction of temporary sterility in the female. If such a means were available, a tuberculous woman, for example, could be tided over the dangerous years of her illness. Should her health subsequently warrant motherhood, the condition of sterility could then be suspended.

Surgical methods of inducing sterility are open to serious objections. When successful, they are generally permanent and fertility cannot be restored subsequently, should the patient's improved health make this course desirable.

Operations aiming to cut and tie the tubes have largely been unsatisfactory, because the stumps are likely to become pervious again at some subsequent time. The surest method of interrupting the passage of the ovum from the ovary to the uterus is by excising the uterine portion of the tube; but, after this operation, fertility cannot be restored.

Turenne[3] has described an ingenious operation to induce temporary sterility. He sutures the fimbriated end of each fallopian tube into a pocket made in the broad ligament. When it is desired to restore fertility, salpingostomy is performed and the lumen of the tube adjusted to the ovary as in the performance of classical salpingo-ovaropexy. Such procedure, however, involving two laparotomies in a woman who presumably is too weak to bear children, would not seem susceptible of employment on a large scale.

BIOLOGIC STERILITY

During the last few years, considerable research has been done with reference to the biologic prevention of conception in female animals. For this purpose, various measures have been employed, including injections of placental extracts and extracts of ovaries of pregnant animals, transplantation of ovaries of pregnant animals into healthy young females, and immunization by parenteral introduction of spermatozoa. The results with reference to the induction of temporary sterility have been most definite following injections of spermatozoa. This topic will therefore receive consideration first.

That animals react biologically to the introduction of seminal products and form a biochemical defense, has been clearly established. Farnum[5] in 1901 injected rabbits with semen in order to ascertain whether they are capable of elaborating specific precipitins for semen. He found that rabbits injected intraperitoneally with semen or testicular emulsion of dog, bull, or man develop specific antisemen precipitins. Hektoen[6] in 1922 demonstrated that the injection of rabbits with human serum induces the formation of precipitins that are specific for human seminal proteins. Waldstein and Ekler[7] in 1913 were able to demonstrate that material from the seminal fluid is absorbed, at least in rabbits. Landsteiner[8] was the first to demonstrate the presence of spermatoxins in blood serum after parenteral introduction of spermatozoa, and his researches have been corroborated by others.

STERILITY PRODUCED BY SEMEN IMMUNIZATION

On clinical grounds, Vogt[9] believes that overloading with seminal products may lead to sterility and that natural fecundity is restored by prolonged abstinence from sexual intercourse. The first cohabitation is the one that is most frequently followed by pregnancy. This may be explained by the absence of immunity of spermatozoa, which is acquired only after intercourse. Van der Dyck states that the blood serum of sterile women in whom no other cause of sterility can be found always belongs to the agglutinating group. Although the assumption of sperm immunity is only a hypothesis, an influence from resorption of sperm has unquestionably been established. According to Mayer,[10] abortion of very young ova may result from frequent coitus after a long period of abstinence.

Tushnov[11] was one of the pioneers in this field. On the basis of his early experiments he asserted that temporary sterility may be induced in female animals by immunization with spermatozoa of a different species. He was very insistent on the use of heterogenous spermatozoa for inducing infertility. His work, like that of most subsequent investigators, showed the injections to be harmless.

Fogelson's results[12] in 1926 showed that we have an accurate method of temporarily inhibiting conception in rats by sensitizing the female to spermatozoa protein. Anello-Rabboni[13] observed sterility after introducing a freshly prepared extract of rabbit testes into doe rabbits. When an extract of guinea pig testes was used, sterilization was not obtained.

By injecting the semen of rabbits or of closely related species, Dittler[14] in 1920 rendered female rabbits sterile for varying periods of time according to the number of injections given. In order to eliminate the possibility of a primary sterility due to other causes, he employed only rabbits which had given birth to at least one litter. It is to be noted, however, that natural sterility in rabbits is rare and that the animals frequently become pregnant after a single copulation. In some cases, examination of the blood serum of the sterilized animals showed it to be definitely toxic to spermatozoa, causing agglutination and inhibiting their motility. Large doses of human semen failed to induce sterility in rabbits. Repeated laparotomies on the animals during the process of immunization against semen showed that the process of ovulation was going on normally. Except for the gradual loss of weight, the animals showed no ill effects from the repeated injections of semen. When numerous injections were given, this loss of weight was more marked. In two cases there was an actual cachexia with atrophy of the sex glands.

Castoro[15] in 1926, in guinea pigs, induced a period of temporary sterility by subcutaneous injections of the seminal products of male guinea pigs. The injections were well tolerated and no anaphylactic reactions were observed in any instance.

McCartney[16] in 1923 injected female rats subcutaneously with spermatozoa suspension. He found that the rats remained sterile for a period of from two to twenty-two weeks beyond the normal gestation time, although the normal sexual cycle and sex behavior of the animal seemed in no way altered. He concludes that the spermatoxins of the immunized animal are present in the vaginal and uterine secretions and have an agglutinating effect on the spermatozoa.

According to McCartney, the degree of immunity is proportional to the amount of spermatozoa suspension injected. After the immunity caused by the injection of the spermatozoa has worn off, the animal is again able to bear normal young.

Guyer[17] in 1922 demonstrated that when male rabbits and guinea pigs are injected intravenously with specific spermatoxic sera obtained from fowls or with the spermatozoa themselves, sterility results and the serum of the animal becomes spermatoxic.

Karasek[18] believes that immunization with spermatozoa offers a great advantage over the usual methods of sterilization now in vogue, since it involves no permanent injury to the sex organs or the body as a whole. Aside from fertilization, it may eventually be proved that the female organism is influenced for the good by absorption of seminal products. Rosenfeld[19] in 1926 reported the results of repeatedly injecting human semen containing spermatozoa into three women. A definite positive test for a spermatoxic principle was not demonstrable, although a complement-binding body was clearly identified. Rosenfeld suggests that it may be possible to regulate the injections so that a sufficient quantity of spermatoxic substance will always be present in the serum.

Bodnar and Kamniker[20] reported tests on the blood serum of one hundred women to determine the effect of the serum on the viability of spermatozoa. They

do not believe that their findings indicate that a diagnosis of "immunity to spermatozoa" can be made by serologic methods in cases of sterility.

Oslund,[21] in 1926, claimed that the delay in pregnancy occasionally found after sperm injection is of short duration and is probably caused by physical disturbances of the body rather than antibody reactions, also that some of the delayed pregnancies reported in the literature were probably due to breeding conditions. This view, however, is contrary to the work of most investigators.

Perhaps the most exhaustive experiments with reference to the biologic induction of temporary sterility in female animals have been performed by Kostromin and Kartashev,[22] of the Perm Institute of Bacteriology, in East Soviet Russia.

As this paper is very difficult to obtain and appears only in Russian, I thought it desirable to quote it at great length for the benefit of the average reader, to whom the material would not otherwise be available.

The government of Soviet Russia recognized economic distress as an indication for the prevention of conception and is sponsoring a considerable amount of research for the purpose of devising a biologic method of contraception applicable to women. In the United States, of course, we are not in sympathy with such a liberal use of contraceptive technic and believe that impregnation should be prevented only when the health of the woman demands this course. Nevertheless, while we cannot countenance the far too liberal application of the prevention of conception by biologic means advocated in Soviet Russia, we must admit that the results of the research work done for this purpose have great scientific value and that we may possibly utilize them to advantage for the control of impregnation under conditions set forth by the physician.

Kostromin and Kartashev began their experiments in 1924 and completed them in 1927. They injected female rabbits and guinea pigs with heterogenous spermatozoa, both living and dead, and obtained positive results in both cases. However, the results were better when living spermatozoa were used. They used spermatozoa from the bull for immunization of rabbits and guinea pigs; and from rabbits for the immunization of guinea pigs; and from guinea pigs for the immunization of rabbits. The experimental results reported by Kostromin and Kartashev are most impressive and offer much encouragement for the clinical application of biologic sterilization in the practice of gynecology. Certainly the results of the investigations so far reported are sufficiently convincing to justify further study with the hope of eventually placing at the disposal of the physician a simple, safe, and convenient method of inducing temporary sterility under circumstances when the onset of pregnancy would endanger the health of his patient. But we must be conservative. To quote an editorial[24] in the *Journal of the American Medical Association*, "Whether injection of spermatozoa or spermatoxic serums may be used as a method of sterilization in human biology is a question of the future." Credit is due to Kolpikov[23] for the preparation of a standardized vaccine containing a definite number of spermatozoa.

STERILITY DUE TO OVARIAN TRANSPLANTS AND HORMONE INJECTIONS

Haberlandt[25] in 1921 attempted to produce temporary sterilization in female animals by transplanting the ovaries of gravid animals. Also experiments performed showed that it is possible to produce a hormonal sterilization of the females by subcutaneous injection of extract of ovaries of pregnant animals.[26] The sterile periods lasted one and a half to three months in rabbits and three to four weeks in guinea pigs. Haberlandt considers that this form of sterilization may be applied

as a therapeutic measure by employing injections of extract of ovary of pregnant animals in order to provide temporary sterilization for prophylactic or hygienic reasons. The ovaries of the treated animals contained numerous small follicles but no large mature ones. It therefore appeared that the treatment had brought about a great inhibition in the maturation of the follicles. Treatment with Abderhalden's placenta opton had the same effect, especially when the material was taken in the second half of pregnancy.

The inhibition took place in three stages: (1) The animal would not allow herself to be covered. (2) The animal could be covered but fertilization did not take place. (3) The animal became pregnant but the number of young was decreased. Haberlandt[27] showed that injections of corpus luteum do not have the effect of interfering with impregnation. In 1927 he produced temporary sterility in white mice by feeding them with ovarian or placental extract over a period of one or two months.[28] The sterility induced thereby lasted from one to two and a half months, which is a long time considering the short life of the white mouse. In some cases, the animals were rendered permanently sterile.

Köhler[29] attributes Haberlandt's experimental results to a nonspecific protein effect rather than hormone action. He injected female rabbits with various organic extracts, including mammary glands, kidney, testicle, and spleen extracts. He observed that the animals resisted intercourse after such injections and did not become pregnant. Whether the organic extract injected was prepared from the ovary or some other gland, temporary sterility was induced thereby in either case.

Greil[30] questions Haberlandt's work with reference to the production of sterility in animals by the implantation of ovaries of pregnant animals and the injection of ovarian extract from pregnant animals. He maintains that there is no proof that sterility in these cases was due to the action of a sex gland hormone, believing that it was caused by a toxic element in the extract used. He asserts that toxic doses of the extract must have been used and is unalterably opposed to the use of such extracts in gynecology.

However, Haberlandt[31] specifically stated that there was no evidence of toxic action in his experiments.

PERSONAL EXPERIMENTS

In the conduct of my experiments, I have largely followed the line of research laid down by Kostromin and Kartashev, believing that confirmation of their findings would be of great value. I employed female rabbits exclusively, as being the most convenient animal with which to work. It is not too small. On the other hand it is cheap, inexpensive to maintain, and easy to house. It copulates readily when mated. There is never any doubt whether copulation has taken place.

A research worker who is not already familiar with rabbits and contemplates repeating similar experiments, should study carefully the books dealing with the care and breeding of rabbits.[32, 33, 34]

Hygienic housing, proper food, and regularity of feeding are of much importance. Lusk[35] states that in undernutrition in rabbits, the reproductive function is one of the first to suffer. Of recent years it has been fully established that a state of infertility may be produced by a diet deficient in vitamine E. Hammond and Marshall[36] assert that the percentage of rabbits which will copulate depends upon the temperature at the time as well as on the abundance of good

and succulent food. The diet is particularly important in winter time; for poorly nourished rabbits will not breed during cold weather, although they would do so on the same diet during the summer. It is therefore necessary to be liberal with the feeding of the rabbits during the winter and fall in order to avoid a spurious sterility really due to seasonal and dietetic conditions.

The spermatozoa were obtained from various species, rabbits, guinea pigs, and sheep. I was particularly interested in the use of sheep spermatozoa for the reason that, if biologic sterilization should prove a success in woman, sheep testes will be readily applicable to clinical use, since they are easily obtained in large quantities. It would also be desirable to use heterogenous spermatozoa to produce immunity in women, since there would be no danger of shortage of material or of transmitting diseases, such as gonorrhea or tuberculosis, as would be the case if human semen were employed.

The sheep testes were obtained from the slaughter house as soon as the animals were killed. They were kept in their capsules in the ice box until used, usually an interval of about four hours. There was no danger of loss of antigenic power from this delay as testes may be kept as long as seven days without deteriorating, providing the temperature be maintained at from 3 to 5° C. I kept sheep testicles on ice for five days, after which the spermatozoa were still living and active. However, for purposes of injection, I never used material more than four hours old. The low temperature prevents decomposition and growth of bacteria. In the case of rabbit and guinea pig testes, the animals may be killed or castrated whenever their glands are needed. It is best to anesthetize the animal, bleed it to death, and then remove the testes, using the epididymis only. By this procedure the gland is rendered anemic and the danger of nonspecific protein effect reduced to a minimum. When immunizing with living spermatozoa, it is better not to use glands older than two to three days.

The capsules of the testes were opened with sterile scissors and the globus major of the epididymis was removed and placed in a Petri dish with normal saline solution. All visible blood vessels were split open and washed thoroughly to remove more completely the nonspecific proteins. Then the epididymis was placed in another Petri dish with normal saline solution and cut into small pieces the size of a pea. These fragments were stirred thoroughly so as to release the spermatozoa from the gland substance into the saline solution, giving rise to a milky emulsion. After this emulsion was filtered through three layers of gauze and diluted to the desired extent, it was ready for injection.

At first unwashed spermatozoa were used. Later the emulsion was placed in centrifuge tubes and rotated for five minutes. The supernatant fluid was pipetted off and the sediment mixed with fresh saline and recentrifugalized. This procedure was repeated three times. The washed spermatozoa were then examined under the microscope and invariably found to be actively motile. Before injection the spermatozoa were placed in an incubator, the temperature of which was gradually raised to 37.5° C. Thus warmed, even the sluggish spermatozoa regained their active motility. If the chemical reaction was other than faintly alkaline, a strong solution of sodium bicarbonate was added until this reaction was produced.

The proper concentration of the suspension for injection is very important. At first the concentration was estimated by a turbidity comparison test, such as is used for roughly counting the number of microorganisms in bacterial vaccines. As

standards of strength, the emulsions were compared with suspensions containing one to two billion bacteria per cubic centimeter. But this method soon proved too uncertain. The most satisfactory method was found to be by actual count in the Thoma-Zeiss chamber. Since our ultimate object is clinical application, it was felt that the dosage should be determined with great accuracy.

The actual number of spermatozoa contained in 1 c.c. of the packed spermatozoal suspension was found to be about 6,000,000,000. This figure was derived as follows: A 1:1000 suspension of sheep spermatozoa counted in the Thoma-Zeiss chamber gave an average of 600 spermatozoa per square. The square has an area of 1 sq. mm. but a depth of only 1/10 mm. Therefore, the multiplication must be by 10 to make 1 c.mm., by 1000 to make 1 c.c., and by 1000 to correct the dilution: $600 \times 10 \times 1000 \times 1000 = 6{,}000{,}000{,}000$.

For purposes of injection a suspension containing 30,000,000 spermatozoa per cubic centimeter was used. Therefore the packed suspension was diluted 1:200. I gave the injections either subcutaneously or intramuscularly, as these will undoubtedly be the routes by which women will receive them, should the method prove of value. Some investigators, including Tushnov, have used the intravenous and intraperitoneal avenues.

While the number of injections, their frequency and the dosage are matters of much importance, it was necessary to be quite arbitrary in these respects, as there are no exact standards to follow. In my experiments I began with a dose of 1 c.c., containing 30,000,000 spermatozoa. The second dose was 2 c.c.; the third, 4 c.c.; and the fourth, 6 c.c. The interval between the injections was two days.

The animals were studied closely and their temperature was taken before and after the injections. There was no noticeable change in their condition or behavior. They ate and behaved just like the control animals and the temperature showed hardly any deviation.

Two or three weeks after the last injection, the immunized animals were placed in a hutch with male rabbits for about one week. This did not prove to be a wise procedure, as the animals do not mate well when kept together and the bucks fight each other. Early in my experiments I lost quite a few animals, particularly males. Although they were much tamer, the does also would fight and several of them were killed in this way. The rabbits were then segregated and the practice of bringing the does to the bucks' hutches followed, the bucks being served with the does at intervals of a few days. This procedure proved far more satisfactory.

The first series of experiments was conducted with unwashed and washed live spermatozoa. Doe rabbits were injected, one set with rabbit spermatozoa, another with sheep spermatozoa, and a third with guinea pig spermatozoa.

For the second series, the same spermatozoa were employed, the only difference being that they were not living but killed by formalin, which not only kills the spermatozoa but also preserves the emulsion and prevents contamination, thus enabling us to stock it up for future use. I found that it is not necessary to use living spermatozoa in order to induce biologic sterility in the female. From the clinical point of view, this is a matter of importance, since the application of injections to women and the preparation of stock solutions would be greatly facilitated if dead spermatozoa could be used as effectively as living ones.

In the preparation of the emulsion of dead spermatozoa the material was centrifuged, and washed three times, just as when living spermatozoa were used. Then an emulsion ten times as strong as would be used for injection was prepared. The spermatozoa were killed with 0.25 per cent formalin; so that, when the material was diluted ten times preparatory to injection, it contained 0.025 per

cent of formalin. This method of preparing the material for injection by diluting a stronger stock solution had two advantages: The stronger formalin solution prevented decomposition and contamination, while the weaker solution proved free from deleterious effects when injected. The injections in the second series were given in the same manner and dosage as in the first.

In the third series only sheep spermatozoa were used. One question which I wished to answer was: Is it necessary to have intact though dead spermatozoa to induce sterility in the female or can the same result be obtained by injecting various substances extracted from spermatozoa?

The integrity of the spermatozoa was destroyed by the following three methods: 1. Sheep spermatozoa were prepared in the same manner as in the first two series. Then 1 c.c. of the packed sediment was rubbed with sterile washed and ignited sea sand in a mortar. Two hundred c.c. of normal saline were added. The mixture was allowed to stand until the sand settled; then the supernatant fluid was poured off. This fluid was passed through a Berkefeld filter.

2. Sheep spermatozoa were triturated with sand as above and 20 c.c. of 95 per cent alcohol added. After thorough mixing, the sand was allowed to settle and the alcoholic solution decanted. From this the alcohol was evaporated by exposure to an electric fan. The remaining sediment was dissolved in normal saline solution and passed through a Berkefeld filter.

3. To 1 c.c. of packed sheep spermatozoa was added 25 c.c. of normal sodium hydroxide solution, which dissolved the spermatozoa so that only small fragments of heads and tails were discernible as faint shadows. This mixture was neutralized with normal hydrochloric acid solution, was diluted to 200 c.c. with normal saline, and was passed through a Berkefeld filter.

These three solutions were placed in sterile containers and kept on ice. Before injection, the required amount of the solution was placed in a thermostat and brought to a temperature of 37.5° C. The dosage and intervals were the same as in the experiments of the first two series.

In all three series, the injections were given either subcutaneously or intramuscularly on the inner surfaces of the thighs, alternating the extremities with each injection. There was not a single severe local reaction or infiltration in any of the groups of experiments.

RESULTS OF EXPERIMENTS

In the first series of experiments, it was desired to ascertain whether intramuscular injections of living sheep and guinea pig spermatozoa, either unwashed or washed, can produce sterility in doe rabbits and how long this sterility may be expected to last. The results of this investigation are given in Table I.

In five of the eleven doe rabbits whose histories are enumerated in Table I, a series of four intramuscular injections of sheep or guinea-pig spermatozoa, either unwashed or washed, produced a period of sterility lasting over six and a half months and still existing at the time when this paper was written. These animals were periodically subjected to intercourse with bucks of proved potency and all of the controls became pregnant; therefore, there can be no question but that the sterility was the result of the spermatozoal injections. Unfortunately four of the animals of the first series died before the duration of their sterility was sufficiently long to be of statistical value.

TABLE I. INTRAMUSCULAR INJECTIONS OF LIVING SPERMATOZOA

NO. OF DOE RABBIT	VIRGIN OR MATRON	SPERMATOZOA	WASHED OR UNWASHED	COMPUTED DATE OF CONCEPTION	DATE OF GIVING BIRTH	NO. OF OFFSPRING	DAYS OF STERILITY	REMARKS
1	V	G.P.	U	----	----	--	82	Died 9/28/27
2	V	G.P.	U	----	----	--	208	
3	V	G.P.	U	----	----	--	208	
13	M	G.P.	W	----	----	--	208	
15	M	G.P.	W	----	----	--	---	Died 7/ 7/27
4	V	SHP.	U	11/ 3/27	12/ 3/27	4	115	
5	V	SHP.	U	----	----	--	64	Died 9/10/27
6	V	SHP.	U	10/28/27	11/28/27	4	110	
16	M	SHP.	W	----	----	--	86	Died 10/ 2/27
17	M	SHP.	U	9/ 3/27	10/ 3/27	2	57	
18	M	SHP.	W	6/ 9/27	7/ 9/27	1	---	Pregnant when injected

Each cubic centimeter contained 30,000,000 living spermatozoa, either guinea pig or sheep and either unwashed or washed, as indicated in the table.

Dosage: First on July 1, 1927—1 c.c.; second on July 3, 1927—2 c.c.; third on July 6, 1927—4 c.c.; fourth on July 8, 1927—6 c.c.

Doe 18 gave birth to one healthy offspring soon after the injections were completed. She was at the beginning of her second half of pregnancy when the injections were begun and it is noteworthy that the injections did not produce abortion, although the possibility arises that they may have been in some way instrumental in preventing a larger litter. In Doe 17 the period of sterility of fifty-seven days is too brief to be considered a successful result. It is interesting that the four pregnancies occurring in this series gave increased litters as the period of sterility was prolonged. The remaining does are still sterile, a period of nearly seven months.

An immunity lasting seven months may not seem significant, unless we consider the relatively short life of the rabbit as compared with the human being. The life of a rabbit is about eight years, and its usefulness as a breeder about four years. Seven months of sterility in a rabbit is therefore equivalent to approximately three years and eleven months in a woman, an appreciable interval of time. It would seem well within the limits of probability that, should biologic sterility prove possible in woman, it will last sufficiently long after the injections to make it of practical value. This state of affairs would apply particularly to such illnesses as tuberculosis, in which a delay of childbirth for several years may be the means of enabling the patient to have a healthy child with relative safety.

In the second series of experiments my aim was to discover whether there is any marked difference when spermatozoa killed with formalin are used instead of the living and active cells. As will be noted in Table II, there were no failures in this series.

The purpose of the third series of experiments was to ascertain whether spermatozoa which were not only dead but whose morpho-

TABLE II. INTRAMUSCULAR INJECTIONS OF WASHED SPERMATOZOA KILLED WITH FORMALIN

NO. OF DOE RABBIT	VIRGIN OR MATRON	SPERMATOZOA—WASHED	NO. OF INJECTIONS	INJECTIONS COMPLETED	COMPUTED DATE OF CONCEPTION	DATE OF GIVING BIRTH	NO. OF OFFSPRING	DAYS OF STERILITY	REMARKS
33	V	G.P.	4	7/27	---	---	---	---	Died 7/31
34	V	G.P.	4	7/27	11/ 3/27	12/ 3/27	3	97	
35	V	G.P.	4	7/27	----	----	--	190	
36	V	SHP.	4	7/27	----	----	--	---	Died 8/10
37	V	SHP.	6	9/28	----	----	--	190	
38	V	SHP.	6	9/28	12/28/27	1/28/28	5	151	
39	M	SHP.	4	7/29	----	----	--	---	Died 8/ 8
40	M	SHP.	4	7/29				188	
41	M	SHP.	6	9/28				188	
42	M	RAB.	4	7/29				188	
43	M	RAB.	4	7/29				118	Died 11/27
44	M	RAB.	4	7/29				188	

Each cubic centimeter of the material injected contained 30,000,000 spermatozoa killed with formalin, derived either from guinea pig, sheep, or rabbit. The first injection consisted of 1 c.c.; the second, 2 c.c.; the third, 4 c.c.; and the fourth, fifth and sixth, 6 c.c.

logic integrity had been destroyed as well were capable of inducing sterility on parenteral injection. The four does injected with spermatozoa extracted with alcohol showed a sterility of from one and a half to two months and then gave birth to practically normal litters. The four does injected with spermatozoa extracted with sodium chloride showed a sterility lasting from two and a half to three months and then gave birth to litters decreased in number. The four does injected with spermatozoa extracted with sodium hydroxide showed a sterility lasting to the present, over four months. From these results it may be concluded that injections of spermatozoa extracted with alcohol and spermatozoa extracted with sodium chloride tend to decrease the number in the litters and the short period of sterility is probably due to a nonspecific protein action as Köhler[29] has suggested in explanation of Haberlandt's results. Injections of spermatozoa extracted with sodium hydroxide have thus far proved to be effectual. As the spermatozoa employed in the third series of experiments were morphologically destroyed and probably also considerably altered in their chemical construction, it is difficult to attribute their action entirely to true antigenic power.

All of the fifteen control does, coming from the same stock and living under exactly the same conditions as the immunized animals and copulating with the same bucks, became pregnant within a month.

SPERMATOXICITY OF THE SERUM

Tests were employed to determine the spermatoxicity of the serum of the immunized does, the control does and also the bucks. Several methods are available for making this test. I employed the simplest, that used by Tushnov. In this test one drop of fresh standardized

emulsion of actively motile spermatozoa is mixed with two drops of the serum to be tested and placed on a hanging drop slide under the microscope.

The blood is obtained from the rabbit's ear either by puncturing a vein and collecting the drops as they form in a test tube or by aspirating it from one of the veins of the ear by means of a hypodermic syringe. As a rule, about 1 c.c. of blood should be withdrawn. It should be put into a narrow test tube, kept in a thermostat, and there allowed to clot. The serum is then pipetted off and centrifuged.

When the hanging drop slide is placed under the microscope, the observer watches for the time when the activity of the spermatozoa begins to be retarded and when it is completely arrested. As the spermatozoa become less motile, they form clumps, gathering with their heads stuck together and their tails extending outward. The length of time required before agglutination takes place varies and does not seem to follow any special rule. There is no apparent change in the morphology of the spermatozoa to account for the loss of motility.

It is difficult to determine the exact time at which motility of the spermatozoa ceases. The approximate length of time required for the serum to inhibit the motility of the spermatozoa was from four to twenty-five minutes. In the case of the serum of one buck, it was a full hour.

TABLE III. SPERMATOXICITY AGAINST VARIOUS SPERMATOZOA

Evidence of spermatoxicity in immunized animals	6 to 23 m.n.
Evidence of spermatoxicity in control animals	5 to 32 min.
Evidence of spermatoxicity in bucks	15 to 60 min.

Spermatoxicity of vaginal secretion was equally inconstant.

A glance at Table III will show that the results of the spermatoxicity tests do not help us in understanding the nature of the biologic immunity induced by injections of spermatozoa. The average spermatoxicity of the immunized animals did not differ considerably from that of the controls. Only the bucks showed any appreciable difference in this respect, their serum being considerably less spermatoxic than that of all the does, immunized and nonimmunized alike.

The results of my spermatoxicity tests support the work of Bodnar and Kamniker,[20] who, after studying the viability of spermatozoa in the blood sera of one hundred women, were unable to find any consistent relationship between the existence of sterility and the spermatoxicity of the serum.

The spermatoxicity of the vaginal secretion in the controls and in the immunized animals before and after the injections was also studied. A loopful of the secretion from the vagina was mixed with two loopfuls of standardized sheep or guinea-pig spermatozoa and examined on a hanging drop slide under the microscope. On the average, it took thirty minutes before the spermatozoa ceased moving in the drop of vaginal secretion. The spermatoxicity of the vaginal secretion in the

various immunized does proved to be so inconstant that no definite conclusion could be reached as to its significance.

A priori one would expect to find the vaginal secretion of immunized rabbits spermatoxic. Djershevsky[37] has shown that the uterine secretions of mares immunized against diphtheria contain antitoxin. Furthermore, in McCartney's[16] experiments on rats, sterility seemed to be due to the presence of spermatoxins in the uterine and vaginal secretion of the immunized animals, since these secretions agglutinated spermatozoa. Tushnov,[11] on the other hand, does not believe that immunity is due to spermatoxicity of the uterine contents, as he did not find the mucus of the uterine cavity spermatoxic. He attributes the immunity to a disturbance of the biochemical relationships of the generative elements.

WHAT CAUSES BIOLOGIC STERILITY?

In the present state of our knowledge, it is impossible to state what causes biologic sterility after immunization with seminal products or ovarian transplants or extracts.

The first possible explanation is that immunization inhibits ovulation. Opposed to this view is the fact that the immunized animal's sexual life is in no way disturbed, except for the sterility. It generally accepts service from the male and goes through the normal sexual epochs. Furthermore, Dittler[14] performed repeated laparotomies upon animals rendered sterile by semen injections and found the process of ovulation to be progressing normally. We can therefore eliminate inhibition of ovulation as the reason for biologic sterility.

Do the semen injections produce degenerative changes in the ovary? Ovaries of various animals have been subjected to careful examination after this method of immunization and no histologic changes have been found as a result of the treatment.

The spermatoxicity of the serum would appear to offer a likely explanation, particularly in view of the fact that rabbits have been proved to elaborate specific precipitins in their blood after injections of semen. However, this subject has been carefully studied and no consistent relationship can be found between the duration of the sterility biologically induced and the strength of the spermatoxicity. In fact, in my experiments I was unable to show that the serum of immunized rabbits is more spermatoxic than that of controls. Bodnar and Kamniker[20] also observed this lack of definite relationship in women suffering from sterility and in virgins.

The most likely explanation is that offered by McCartney,[16] who found active spermatoxicity of the uterine and vaginal secretions in immunized rats. He believes that the spermatoxins act in the genital tract by killing the spermatozoa introduced by normal coitus and thus preventing impregnation. Tushnov,[11] however, could observe no sper-

matoxicity of the vaginal secretions of rabbits; the results were too variable to have any significance.

Until more evidence is brought forth, it is impossible to reach a conclusion as to the cause of sterility biologically induced.

SUMMARY

Artificial production of sterility is a subject of much importance to the physician who is called upon to advise married women who are physically unfit to bear children. Under such circumstances, there is general agreement that the patient should be instructed with regard to contraceptive technic or, if pregnancy should ensue, that a therapeutic abortion should be induced.

The mechanical means of contraception generally practiced are decidedly inconvenient and, to a certain extent, unreliable, and none of them permits anything like normal sexual relations. While they do not cause serious disturbances of the genital organs, the lack of full consummation cannot but be harmful to the nervous system.

Surgically induced sterility, too, is subject to decided disadvantages. With most operations, the condition of sterility is permanent. Although remediable sterility may be induced by the operations described by Sellheim[4] and Turenne,[3] respectively, these procedures involve two laparotomies on a woman who presumably is too sick to bear children.

Although still in the experimental stage, biologic immunization of the female organism to seminal products offers great promise of clinical application as a means of inducing temporary sterility. Should this method prove successful in human subjects, it will possess obvious advantages. It will enable many women suffering from temporary incapacity to postpone childbirth until such time as they may be physically fit for this function. And, since the equipment will be entirely in the hands of physicians, it can be used only for *therapeutic* purposes.

The most promising method by which artificial biologic sterility may be produced in animals is by the injection of spermatozoa derived from the same or another species. Numerous independent investigators have obtained positive results in experiments on this subject. In my own experiments, rabbits immunized by injections of sheep or guinea-pig spermatozoa are still sterile after nearly seven months. The most effective results would, of course, be expected from the injection of living and active spermatozoa; but I also used spermatozoa killed by formalin and also spermatozoa morphologically destroyed and probably likewise chemically altered by three different processes. The rabbits injected with dead spermatozoa are still sterile after nearly six and a half months.

Sterility has also been induced by Haberlandt and other workers by transplanting the ovaries of pregnant animals of the same species

and also by the injection of ovarian extracts. This, too, is a subject calling for further investigation and offering clinical possibilities.

The mechanism by which biologic sterility is produced is unknown. When the temporary period of sterility has passed, the animal is again able to bear healthy young. It has been fully established that the ovaries are not damaged and the process of ovulation is not disturbed by the artificial induction of biologic immunity. With regard to spermatoxic properties induced in the serum by the spermatozoal injections, I found no consistent differences between the sera of the immunized and the control does, respectively. Other investigators, likewise, have been unable to demonstrate any definite relationship between the spermatoxicity of the serum and the duration of sterility biologically induced. It has been suggested that the injection of spermatozoa is followed by the appearance of spermatoxic substances in the vaginal secretions, which either destroy the spermatozoa introduced at copulation or inhibit their motility. While I was unable to find evidence of spermatoxic substances in the vaginal secretions of the rabbits which I immunized to spermatozoa, I admit the possibility of this hypothesis.

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303 West One Hundred and Sixth Street.

LEIOMYOSARCOMA OF THE UTERUS

Report of a Case, With a Brief Review of the Literature

By Earl C. Sage, M.D., F.A.C.S., and A. J. Miller, M.D., Omaha, Neb.

MRS. M. T., colored, referred to me by Dr. J. B. Hill of Omaha, entered the Methodist Hospital, December 20, 1927, complaining of an abdominal enlargement, severe and constant abdominal pain, especially in the lower abdomen; foul bloody watery vaginal discharge; shortness of breath; and a fever of 101° to 103°. Patient was said to be about forty-six years of age, but she did not know when she was born, and appeared to be fifty-five to sixty years of age.

More than ten years ago, patient first noticed the abdominal enlargement, which has gradually increased in size. During the past two years, she has had more soreness and pain in both lower quadrants of her abdomen, and almost a continuous profuse, foul-smelling, bloody or watery vaginal discharge.

During the past year, there has been no regular menstrual flow, and the patient does not know when she had the menopause.

During the past three or four months, she has been frequently nauseated and has vomited at times. The pain in the lower part of the abdomen has increased in severity and has been present most of the time. Patient has been married three times and was never pregnant.

Physical Examination.—Patient is sitting up in bed to relieve pain in her back, looks ill, has some difficulty in breathing. Temperature at present 96.6°, pulse 84, blood pressure 130/74. Positive findings in physical examination.

Head.—Gray hair around temples; pterygium on both eyes; upper teeth false; many teeth missing in lower jaw.

Chest.—There is an area of impaired resonance at the angle of the right scapula, where the breath sounds are less distinct and where moist râles are heard. Heart is not enlarged, but a systolic murmur is heard at the apex of the heart.

Abdomen.—The size and shape of the abdomen are similar to a patient with a full-term pregnancy. A hard mass is felt extending from the pelvis to the costal borders, with tenderness elicited over the entire lower abdomen. Hard, irregular nodules can be palpated through the rather thin abdominal wall, and the whole mass is somewhat irregular in outline.

Vaginal Examination.—A foul-smelling, purulent, sercsanguinous discharge is seen at the introitus. When the examining fingers reach the cervix, it is found to be effaced and dilated as you would expect in a patient who was in labor. Through this dilated cervix can be felt soft, mushy, necrotic pieces of tissue, which can be brought out through the cervix with the fingers. Some of this material was saved for section and microscopic study.

Laboratory Findings.—R.B.C. 4,180,000, W.B.C. 10,300. Hb. 75 per cent. Differential 84 polys., 16 lymphocytes. Wassermann 2-plus.

Preoperative Diagnosis.—Fibromyoma of the uterus with malignant degeneration and suppuration; bronchitis.

X-ray Examination of Lungs.—Fluoroscopic examination of thorax revealed very diminished excursion of diaphragm on both sides. The costophrenic angles were clear. Apices aerated on coughing. Increase in hilum shadows on both right and left sides, with more on the right. The cardiac shadow was normal.

Stereoscopic films corroborated the fluoroscopic findings. There was considerable increased density of the hilum on both sides, conforming more or less to the

ramifications of the bronchovascular tree at the root of the lung. There was no evidence of parenchymal involvement at the present time, which could account for her elevation in temperature.

Dr. C. B. Peirce, roentgenologist, was inclined to regard the hilum shadows as suspicious, until proved otherwise, rather than a suggestion of malignancy. They could be due, of course, to old tuberculous infection. There was not visible at this time, any evidence of parenchymal metastases.

Even though the patient was a poor operative risk, since her condition was not compatible with life, an operation was planned. The patient was running a septic temperature, as Fig. 1 will show, she had the characteristic metrorrhagia and watery discharge for two years, she was in constant pain, and decided to take the risk.

The patient was operated upon January 5, 1928, a midline incision was made from the symphysis to one inch above the umbilicus. There were some adhesions to the fundus and posterior wall of the uterus, extending to adjacent coils of small intestine. After freeing these a complete hysterectomy was performed. The malignant growth had evidently extended into the broad ligaments and pelvic walls as myxomatous tissue was cut through in freeing the uterine tumor mass.

The patient exhibited signs of shock as the tumor was removed, normal saline was administered under the breasts and caffein sodium benzoate given hypodermatically.

After the peritoneum was sutured, the other layers of the abdominal wall were quickly closed with interrupted silkworm-gut sutures.

The patient made an uneventful postoperative recovery; there was primary union of the wound and her temperature dropped to normal on the third postoperative day. She was out of bed on her fifteenth postoperative day, and walking around the ward at the end of three weeks.

She has some swelling of the axillary glands on the left side, and her left arm became swollen on the eighteenth postoperative day, and another x-ray examination of her lungs was ordered to ascertain whether metastases could be shown. X-ray examination of lungs on the nineteenth postoperative day showed the following.

X-RAY REPORT

Fluoroscopic examination of the thorax revealed a good excursion of the diaphragm. Costo-phrenic angles clear. Heart shadow within normal limits. The hilum is increased on both sides with a suggestion of round masses of increased density in the hilum and one or two in the outer lung fields, particularly on the right side.

Stereoscopic films of the thorax demonstrate a fairly symmetrical thoracic cage. Domes of the diaphragm are smooth. Costo-phrenic angles are clear. Cardiac shadow normal. Hilum shadows increased on both sides with soft increased markings of the broncho-vascular tree, particularly on the right side, but somewhat to the left. In the

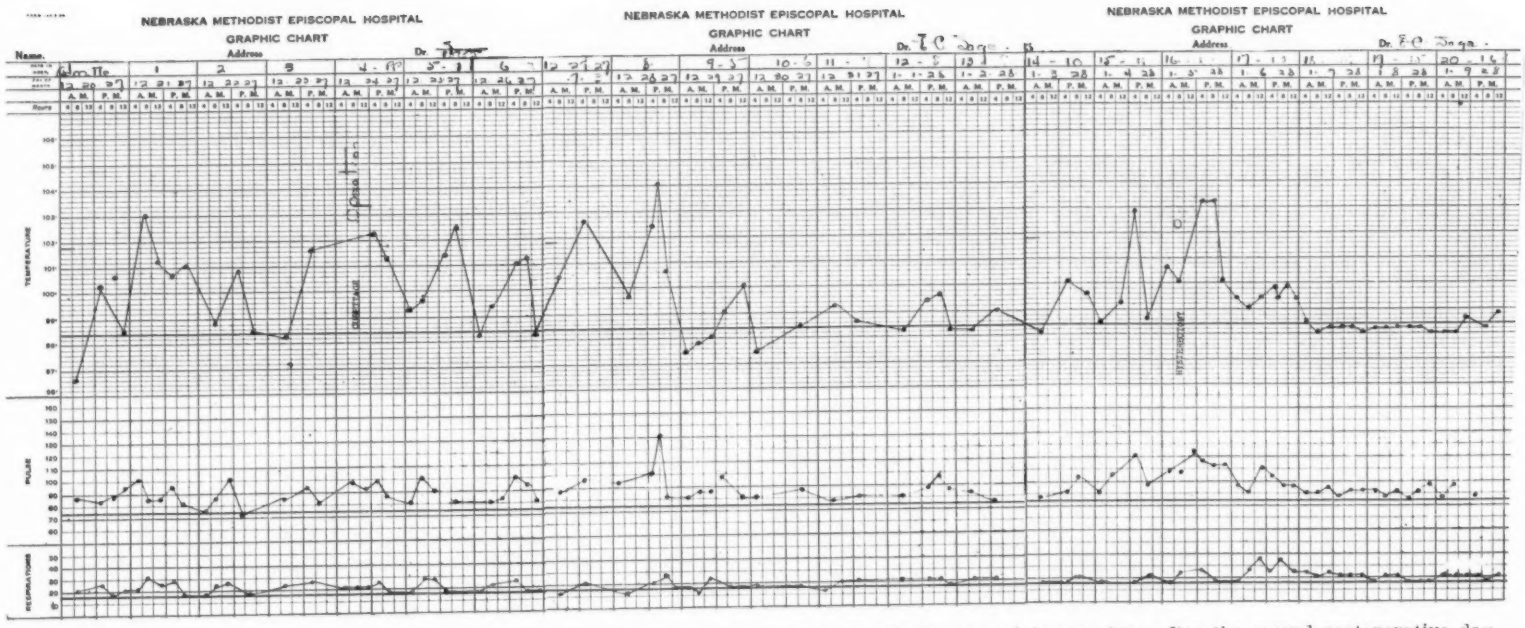

Fig. 1.—Temperature chart showing septic temperature before operation and practically normal temperature after the second postoperative day.

hilum there is suggestion on the right side of some round masses very similar to those previously observed. Some thickening of the apical pleura, particularly on the left with slight irregularity of its shadow. Beneath the inferior angle of the right scapula there is observed a round area of increased density quite soft in character, apparently lying in the outer lung field which would suggest from its contour and density, a neoplastic growth. I do not find any other areas which are so peculiarly suggestive. I still do not feel that we can say absolutely that there is a pulmonary neoplastic metastasis.

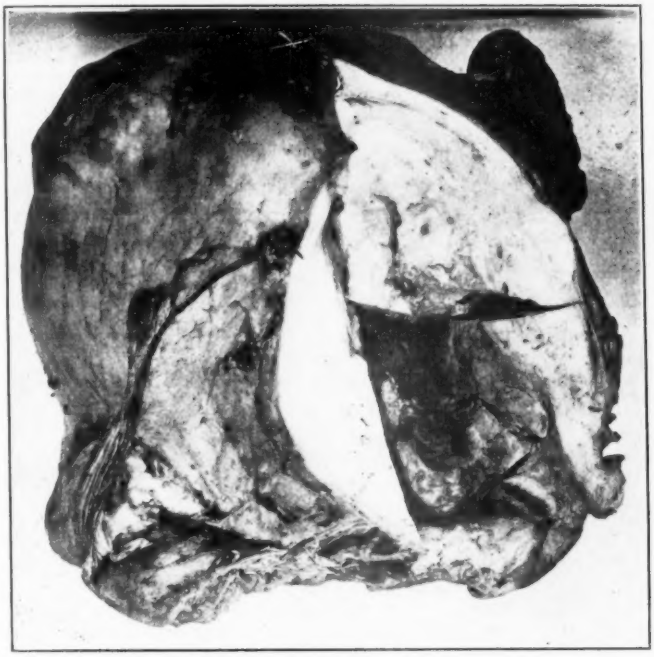

Fig. 2.—Gross specimen. Nodular uterus measuring 16 by 18 by 20 cm. with adnexa attached. Cervix was dilated two fingers. Necrotic mass shown just above cervix.

METASTASES

In this connection, it is interesting to note that Ewing has only encountered three malignant uterine myomas with general metastasis and two with local recurrence in twenty years, and Winter found no case among 753, so that malignant degeneration of myoma must be rare.

However, a rather numerous group of cases of leiomyoma are on record, which have proved malignant, breaking the natural boundaries and producing metastases in liver, lungs, kidney, peritoneum, and lymph nodes, and thereby acquire the designation "myoma malignum."

In Evans' series of 72 malignant fibromyomas in a series of 4000 operations for uterine fibromyomas at the Mayo Clinic, definite indica-

tions of metastases to distant organs were not found in any of these cases. From the findings at operation and from the subsequent histories of the fatal cases there was evidence of extensive and local abdominal metastases. He states "As compared with other types of malignant tumors, nonepithelial uterine tumors are said to be comparatively low grade in malignancy. This seems to be true in so far as metastases in distant organs are concerned. But from the standpoint of rapid and extensive local infiltration, these tumors must be classified as extremely malignant.

The report of the study of the tumor mass is as follows:

Gross Examination (Fig. 2).—The specimen consists of a symmetrically enlarged but somewhat nodular uterus measuring 16 by 18 by

Fig. 3.—Specimen of uterus cut in half, showing the malignant degeneration occupying practically the entire uterus. On section the lumen is filled with foul-smelling necrotic greenish yellow tags of tissue, which on section proved to be leiomyosarcoma.

20 cm. with the adnexa attached. On section the lumen is filled with foul-smelling, necrotic, greenish yellow tags of tissue. The tumor weighs 5½ pounds. The necrotic area measures about 15 cm. in length and 7 cm. in width. From the picture of the cross-section, it is seen that the degenerated area occupies a large portion of the fibroid tumor. (Fig. 3.)

Pathologic Examination, Dr. A. J. Miller.—The sections are made of uterine wall; the inner portion of which is replaced by neoplastic tissue. This is made up of long spindle cells with eosin staining cytoplasm, shaped much like normal muscle fibers. In portions, however, these cells are polygonal but they still have eosin staining cytoplasm.

The nuclei of the elongated cells are also elongated and resemble greatly the nuclei of muscle cells, except that they are larger and have more chromatin material. The nuclei of the polygonal cells are very irregular but they tend to be round. Chromatin material varies much in its arrangement and density. Mitotic figures are abundant in these cells and are occasionally found in the spindle cells. There are quite a number of giant cells. There are a number of atypical mitoses, consisting of irregular or multipolar spindles. There is in different sections a rather imperfect gradation between the cells which very definitely resemble uterine muscle and the large polygonal cells which resemble surface cells more than muscle.

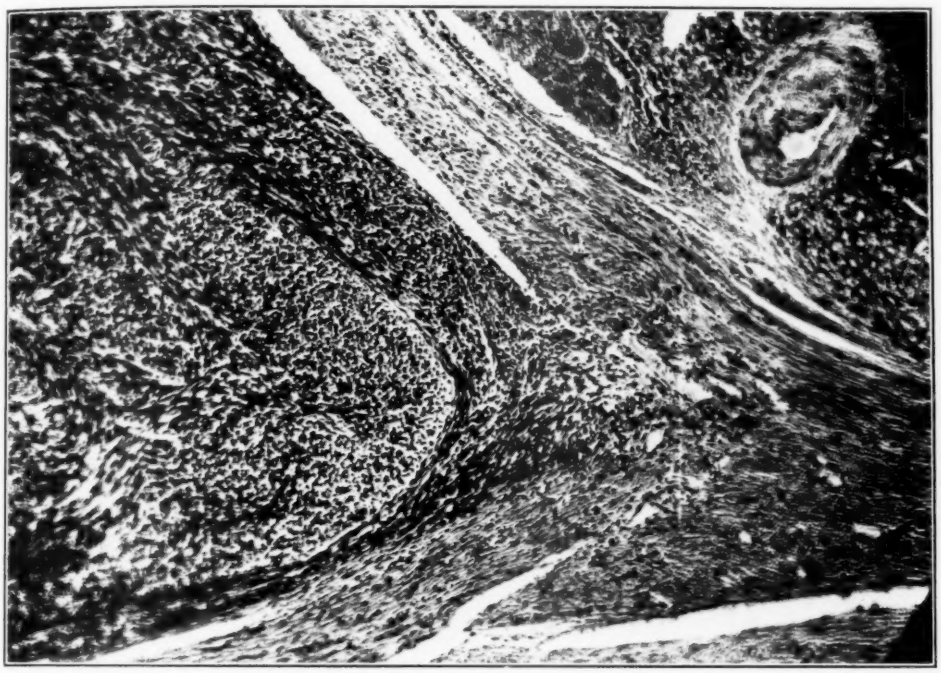

Fig. 4.—Photomicrograph of spindle cell tumor tissue resembling myometrium invading the wall of the uterus. (Low power.)

The first impression of these polygonal cells was that they were possibly epithelial derivatives or syncytial masses. This view was no doubt in error. The malignant nature of the neoplasm is definitely demonstrated at the periphery where the new growth is destroying the muscle tissue and also in several places, has invaded blood vessels.

Sections were submitted to Dr. F. B. Mallory, Boston City Hospital, who replied, "Your tumor is unquestionably a very pretty leiomyosarcoma."

Sections were also submitted to Dr. S. B. Wolbach at Harvard Medical School who replied, "For awhile I wondered whether possibly you had something in the way of a mixed tumor with striated muscle ele-

ments suggested by the large cells, but I could find no proof of this, and I do not regard the cells as incompatible with smooth muscle tumor. I think you are dealing with a very rapidly growing malignant leiomyoma or leiomyosarcoma." (See Figs. 4, 5, 6, 7, 8, and 9.)

There are two views as to the origin of this tumor: One that it is a leiomyosarcoma, or smooth muscle tumor which has been malignant from the start; the other that it is a malignant leiomyoma, or a "fibroid" that has become malignant. The latter view is the most commonly accepted.

According to MacCallum, malignant tumors spring out of benign myomas which have already existed for a long time, but the question

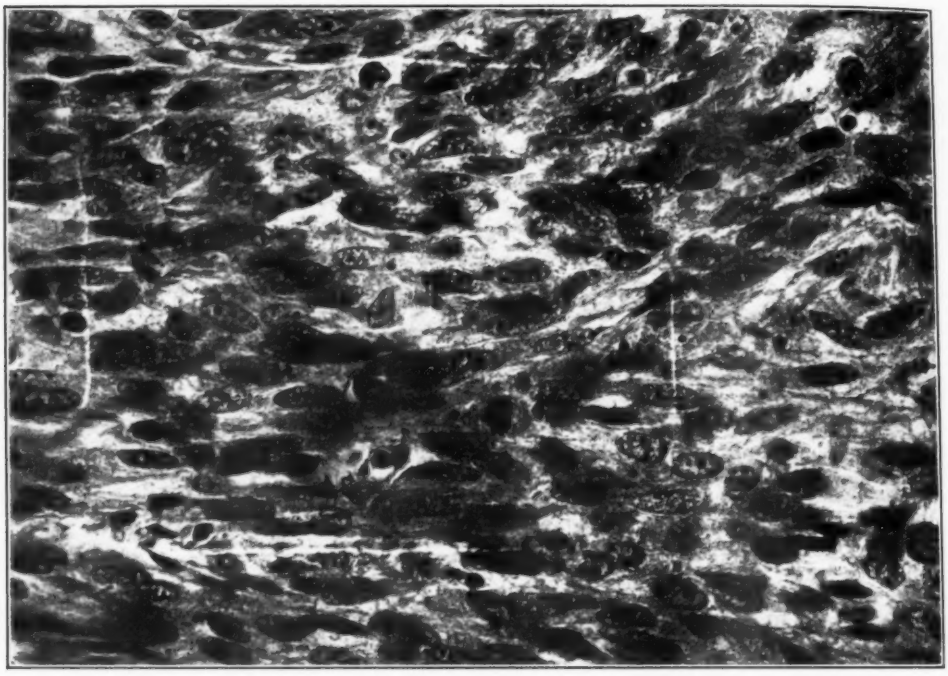

Fig. 5.—Photomicrograph of the spindle cell tumor tissue shown in Fig. 4. The cells are all similar in type, have eosin staining cytoplasm similar in shape and staining reaction to the plane muscle in the uterus. In this portion of the tumor there is but one type of cell. One mitotic figure is shown near the center of the field. (High power.)

remains as to their exact origin. They may be due to the acquisition of malignant powers of growth by the smooth muscle cells, in which case we should speak of them as malignant myomas, or the invasive tumor may be the offspring of the stroma of the myomas, and then it would be justifiable to call the tumor a sarcoma. It is only in the latter case, in which there is a true sarcoma mixed with muscle tissue of the myoma, that such a term as myosarcoma is justifiable. A sarcoma is not a tumor derived from muscle, but rather one arising from connective tissue.

Further History.—On February 18, 1928, I was notified that the patient died at her home forty-five days after the operation. After receiving the pathologic reports, we told the family that we did not feel the patient could live over two months. The exact cause of death could not be ascertained, as autopsy was not permitted, so the extent of the metastases will never be known.

TABLE I. FREQUENCY OF NONEPITHELIAL MALIGNANT UTERINE TUMORS AS COMPARED WITH FREQUENCY OF FIBROIDS (FROM EVANS)

	FIBROIDS		MALIGNANT	PERCENTAGE	
Proper and Simpson	357		22	6.00	
Miller	9750			1.96	
Lewis	1518			1.40	
Olshausen	6470			1.30	
Kelly and Noble	2274			2.00	
Winter	500			3.20	
Winter	253			4.30	
Noble	337		2	0.60	
Kelly and Cullen	1400		17	1.20	
Martin	205		4	1.90	
Fehling	109		8	1.90	
Broun, Woman's Hosp., New York	1500		7	0.40	
Warner	100				
Including all "cellular"			7	7.00	
"Sacroma" only			2	2.00	
Geist	250		12	4.80	
Series at Mayo Clinic	968	Group 1	6	0.62	
1917 to 1918		Groups 1 and 2	12	1.25	
		Groups 1, 2, and 3	38	4.00	
1906 to 1918	3297	Group 1	13	0.39	
		Groups 1 and 2	22	0.67	
Winter, Henkel, Hofmeier, and Flantan	1880		46	2.5	sarcomatous
Cullen	1200		17	1.4	sarcomatous
Bland-Sutton	500		8	1.6	
Lockyer	210		2	0.9	
Blank	188		2	2.1	

TABLE II. FREQUENCY OF EPITHELIAL MALIGNANT TUMORS AS COMPARED WITH FREQUENCY OF FIBROIDS

	FIBROIDS	MALIGNANT	PERCENTAGE
Bland-Sutton	500	8	1.6
Kelly and Cullen	1000	18	0.9
Blank	188	4	2.1

As Evans points out, the frequency of mitotic figures forms the only safe histologic criterion on which to base a diagnosis of malignancy or "near" malignancy.

Incidence of malignancy of the Mayo series of 1.8 per cent.

In some of the numerous collected series of cases of uterine fibromyomas, the relative proportion which shows malignant change is given as low as 0.4 per cent; in others it is as high as 10 per cent.

Maroney states that the diagnosis "must be a matter of individual interpretation in suspicious cases." Evans' article attempts to make such comparisons of the histologic findings and the clinical histories of the 4000 cases available as will serve to contribute something to the establishment of microscopic criteria, in

view of the evident lack of knowledge and lack of acceptance of uniform standards of malignancy as well as degrees of malignancy in this class of tumors.

A composite picture of the characteristics, as has been presented in the writings of several authorities, includes the following points:

1. Increase in size of tumor cells, as compared with normal muscle or benign muscle tumor cells.

2. Shorter and plumper cells with nuclei more nearly oval than normal muscle or benign muscle tumor cells, rounded, and "vesicular" nuclei.

3. Inequality in size and irregularity in shape and arrangement of the cells.

4. Lack of "differentiation" of cells.

5. Unequal staining of nuclei, and deeply staining nuclei.

6. Presence of immense cells (protoplasmic plaques) with hyperchromatic, single, or multiple nuclei (giant cells).

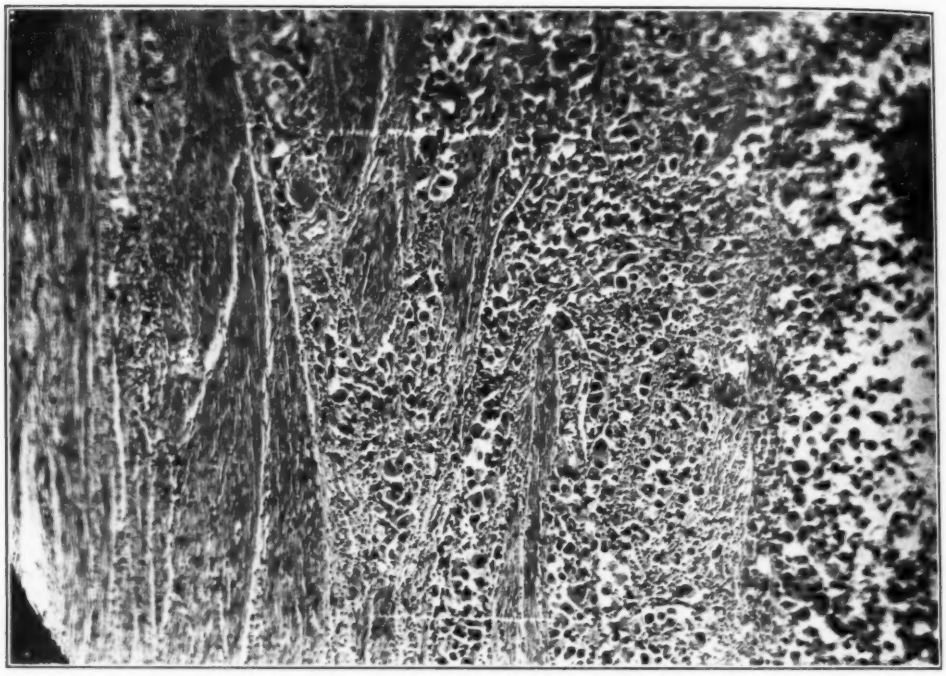

Fig. 6.—Photomicrograph of a different portion of the tumor showing it to be a different type. Large irregular polygonal cells are invading the wall of the uterus. Near the center of the field one invading blood vessel is shown. There are many bizarre cells and mitotic figures. (Low power.)

7. Presence of mitotic figures, typical and atypical.

8. Decrease or absence of stroma fibers between the cells.

9. Thinness or absence of vessel walls.

Proper and Simpson, of the New York State Cancer Laboratory, in their article on "Malignant Leiomyomata" say in substance that the presence of the large irregular nuclei and giant cells is in direct proportion to the degree of malignancy and is an important accompaniment of the malignant process. In doubtful cases they depend on the absence of mitotic figures as the criterion of a benign tumor.

Mallory believes that the presence of mitotic figures in these myomas is a definite indication that they are capable of infiltration and are, therefore, malignant. Lockyer in his volume on fibroids, says that malignant myomas are often difficult

to distinguish and emphasizes the tendency to infiltrate and the presence of mitotic figures as a distinguishing characteristic.

The most important microscopic features aside from the frequency of mitoses are according to Evans:

1. The large size of the great mass of the tumor cells in the given case, and a marked inequality in their size. In those very malignant tumors which are characterized by this type of cellular structure, many abnormally large mitotic figures are apparently invariably found.

2. The relative decrease in the amount of fibrous stroma.

3. The growth among the tumor cells of blood vessels with very thin walls or with walls entirely wanting.

4. The relative increase in the size of the nucleus of the tumor cells as compared with the mass of the cytoplasm of the cell body.

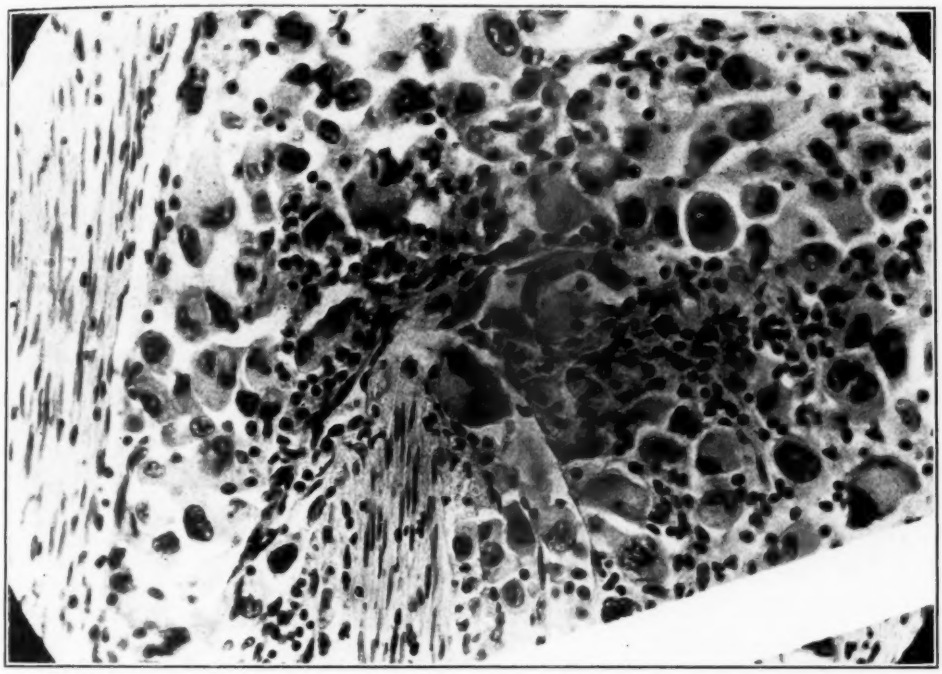

Fig. 7.—Photomicrograph of the same field as Fig. 6 showing the thin-walled blood vessels with several tumor cells in its lumen. (High power.)

While all these changes are important, careful study shows that none is constant, that is, invariably present in the very malignant tumors and always absent in those not malignant. Notwithstanding this fact, it is well to note that the tumors composed of a mass of closely packed cells of very large size are invariably extremely malignant, although it is not true that all the malignant tumors have this particular morphology.

There is evident need of the establishment and recognition of histologic standards of malignancy in the classification of the nonepithelial uterine tumors.

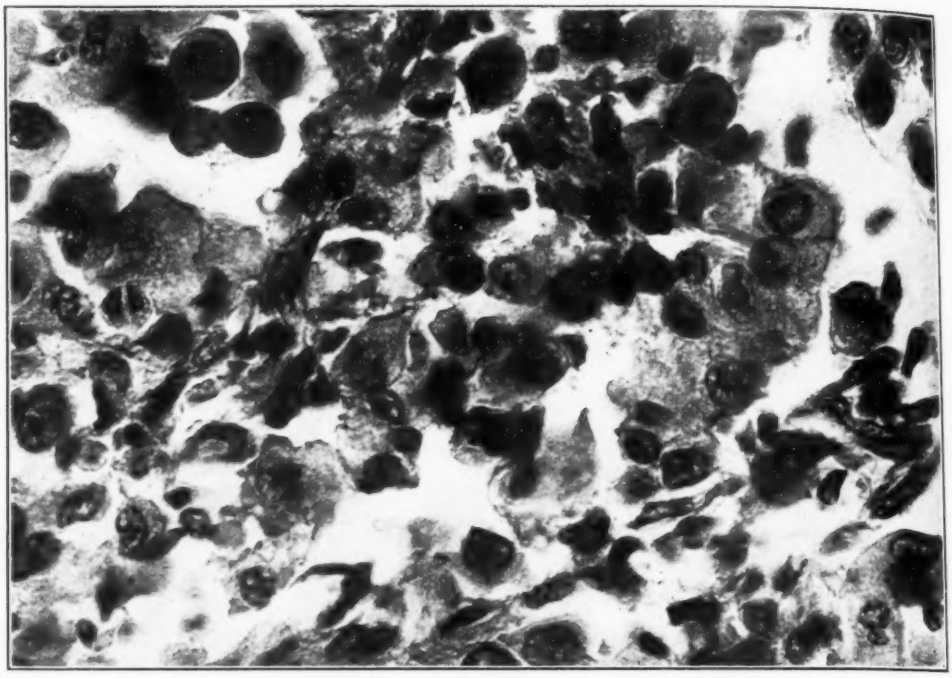

Fig. 8.—Photomicrograph of the central portion of the tumor showing the type of cell to be similar to that in Figs. 6 and 7 but different from that in Figs. 4 and 5. Here the cells are flat, polygonal, have a small amount of new connective tissue stroma, and show no tendency to form the spindle shaped cells. Near the center of the field is a mitotic figure in which the spindle is imperfectly shown. (Low power.)

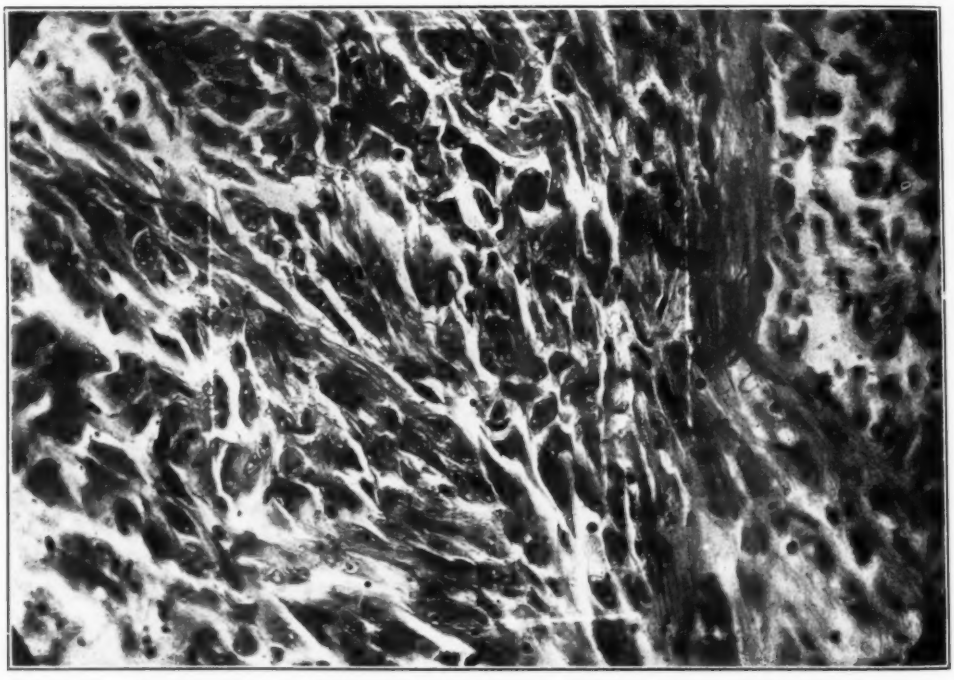

Fig. 9.—Photomicrograph of a different portion of the tumor showing both types of cells in one field. Large irregular polygonal cells are intermingled with spindle-shaped cells which are definitely muscle derivatives. This picture is taken mid-way between portions of the tumor that was composed of spindle cells only and other portions of flat polygonal cells only. There was definite gradation between the two. (Low power.)

In the present study the only single constant microscopic evidence of definite malignancy is the invasion of normal tissue. There are also many atypical cells and abnormal mytoses.

Many of these tumors have numerous large giant cells with multiple hyperchromatic nuclei which are often looked on as evidence of malignancy, but they do not contain mitotic figures. There is no evidence that such tumors are malignant.

In the less malignant tumors not containing numerous mitotic figures there are morphologic evidences of division of tumor cells by direct cell division.

Clinically the majority of patients with definitely malignant tumors present themselves for treatment about the climacteric or later. The tumors are difficult to distinguish in the earlier stages from ordinary fibromyomas; they are not cured by x-ray or radium, and the surgical removal of all fibroids of any appreciable size seems to be the best treatment.

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CHOLECYSTOGRAPHIC STUDIES IN PREGNANCY

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RADIOGRAPHIC studies of the gall bladder in the human subject, following the intravenous injection of the halogenated phenolphthaleins after the method of Graham and Cole, have stimulated a renewed interest in the pathogenesis of cholecystitis and cholelithiasis. For an extremely long time pregnancy has been considered as a contributing etiologic factor in the production of gall bladder disease. We were impressed with the idea that this method of examining the gall tract might disclose the occurrence of functional alterations in the course of pregnancy. If such were found, we believed that they might perhaps lead to more exact deductions as to the bearing of pregnancy on the production of gall bladder disease. We, therefore, studied a series of twenty-two pregnant women. The cases were unselected and consecutive, except for the elimination of those in whom there were grounds for thinking that the patient might incur any risk from cholecystography.

In the study we carried out the procedure on all cases having any signs or symptoms of the toxemia of pregnancy. These were four in number. They were of particular interest as we wished to discover whether, in toxemia, the determination of liver function by estimation of the dye retention in the blood stream, combined with cholecystography, is a more delicate indication of decrease of liver function than the dye retention test alone. Subsidiary to this was the question of the relative value of sodium phenoltetraiodophthalein and the other dyes employed in testing liver function.

There were several other directions in which we hoped data of value might be found. The first of these was to determine whether cholecystography was a safe procedure in pregnancy. If it proved to be so, could it contribute anything to the diagnosis of biliary tract disease in pregnant patients suffering from such affections? We desired to know whether cholecystographic findings in pregnancy varied from those in the nonpregnant state. If variations were found, we wished to discover their nature and degree, the time of pregnancy in which they occurred, and the degree of variation at different periods.

Recently Mann and Higgins[1] have studied the effect of pregnancy upon the emptying time of the gall bladder. For their experiments they employed dogs and gophers (chiefly the latter). Pregnant animals were given a fat meal, the abdomen was opened shortly afterward and the size of the gall bladder observed. The animals were not

examined by cholecystography. These authors expressed the opinion that the contractile mechanism of the gastrointestinal tract as a whole is retarded in pregnancy; further, that the gall bladder either does not empty or does so only slowly. They thought that the increase in volume of the abdominal contents was a causative factor in producing the delay. However, they say nothing about the same factor causing delay in the *filling* of the organ. They infer stasis of bile in the gall bladder, and conclude that it originates from both mechanical causes and defective contractility, and that this stasis is contributory to the production of gallstones in the human subject.

We were also interested in the question of the diffusion of cholecystographic dyes through the placenta, and all cases were scrutinized for the appearance of a fetal gall bladder image.

In all the tests the sodium salt of phenoltetraiodophthalein was employed, in the dose and after the method described by Graham, Cole, Copher and Moore.[2]

When cholecystography was carried out postpartum, it was done within fourteen days, except for one case done six months later. The method of making the liver functional test with sodium phenoltetraiodophthalein is quite similar to that employed in using phenoltetrachlorphthalein or bromsulphthalein. Retention of less than 12 per cent of phenoltetraiodophthalein in the blood serum one-half hour after intravenous injection, and less than 4 per cent one hour after, is considered normal, and also if the sum of the one-half hour and hour specimens gives a retention of 16 per cent.

Of the twenty-two cases, four were toxemic and the test was carried out in the twelfth, fourteenth to sixteenth, and two in the fortieth week of gestation. One of these was of such severity that death ultimately resulted in spite of abortion and all treatment. Three patients had a dye retention of from 5 to 10 per cent, but had no signs of toxemia. We have no explanation for this retention. Cholecystography was a failure in one patient because of her enormous size. One patient clinically had cholecystitis. Subtracting these from the total, leaves thirteen apparently normal cases in which there were neither gall bladder symptoms, toxemia, nor dye retention in the blood stream. In this group, six had a non- and two a faint visualization; i.e., eight of the thirteen cases had abnormal cholecystograms and only five of that number, or 38.4 per cent of apparently normal patients gave normal cholecystograms. Three of these were in the thirty-sixth to fortieth, one at the twentieth, and one at the twelfth week of gestation.

It is apparent that an explanation must be sought for the non-visualization of the gall bladder in the eight normal cases. There are several possible reasons for this occurrence. The gall bladder may not fill because of increased intraabdominal tension or pressure on the

organ or its ducts, or pregnancy may so affect the vesicle that it is unable to concentrate the bile. In regard to the first of these two possibilities it is to be noted that though there were five normal cases with nonvisualization of the gall bladder in the thirty-fourth to fortieth week of gestation, there were also three similar cases with normal cholecystograms. This seems to indicate that the mechanical factor of increased intraabdominal pressure, general or local, if a factor at all, is certainly a most inconstant one.

If the gall bladder loses its function of concentrating the bile in the late months of pregnancy, it certainly regains it very rapidly, as shown by the fact that in two cases there was nonvisualization of the gall bladder before, and normal visualization of the organ after delivery, and by two cases which were normal both ante- and postpartum. Our experience with cholecystography in conditions other than pregnancy has shown that if the concentrating function of the gall bladder is lost it is not quickly regained, and when this does take place it occurs after a greater lapse of time than fourteen days.

For the explanation of the nonvisualization of the gall bladder in the normal cases we fall back on the technical difficulties of radiographing a pregnant woman near term. Whatever poses one may employ for this purpose, a large volume of tissue and fluid must be traversed by the x-rays, with the resulting scattering which produces loss of definition. The increased volume of the abdominal contents is another important obstacle from the technical standpoint as it causes the distance of the gall bladder from the film to be increased. The foregoing influences, either singly or combined, can easily render radiography of the dye-filled gall bladder impossible. Our conclusion is that this accounts for the nonvisualization of gall bladders in the normal cases. This belief is strengthened somewhat by the fact that in the smaller subjects the gall bladder was more readily visualized than in those who were larger. A few cases (four) in the first half of pregnancy were readily radiographed and constantly showed normal cholecystograms. For this reason we would incline to the belief that it is abdominal size, and not month of gestation or intrinsic change of the gall bladder, which brings about its nonvisualization.

In the cases of toxemia, the combination of the dye retention test in the blood and cholecystography was not found to be more sensitive or valuable than the dye retention test alone. The fatal case of severe toxemia with 50 per cent dye retention in the blood and with a good visualization of the gall bladder, would indicate that the damage to liver function produced by this condition would have to exceed 50 per cent in order greatly to influence cholecystography. The few cases incorporated in this report indicate that the toxemia of pregnancy does not affect the concentrating function of the gall bladder as revealed by this method of examination.

In none of our cases was a fetal gall bladder observed. This suggests that the cholecystographic dyes do not pass through the placenta. In a case of precipitate labor the dye was injected ten minutes before delivery; examination of the blood from the umbilical cord showed no traces of the presence of dye.

The cases in which there was visualization of the gall bladder do not correspond to the findings of Mann and Higgins[3] as to delay in emptying of the gall bladder nor any other indication of stasis. However, measure of the emptying time of the organ by the use of the fat meal was not carried out.

Where the gall bladder was visualized, the organ corresponded in every respect to that observed in the nonpregnant state, except for modification of its position and the changes incident thereto. Because of the increase in volume of the abdominal contents, the gall bladder assumes a higher and somewhat more lateral position, just as one would anticipate, the degree of this change being proportional to the abdominal size.

The one case of clinical cholecystitis included in the series behaved precisely as a case with such a history and symptoms would do if nonpregnant.

We were unable to find any essential difference in the functional activity of the gall bladder in pregnancy as revealed by cholecystography. We believe that the frequent occurrence of nonvisualization of the gall bladder is due to the radiographic difficulties mentioned above. Accepting this explanation of nonvisualization, the gall bladder has normal ability to concentrate, shows those alterations usually observed in cholecystography of normal subjects, and empties within the usual time.

Sodium phenoltetraiodophthalein is of equal, if not superior, value to the other dyes used in estimating liver function, but largely because of the fact that a greater amount of this dye is employed.

CONCLUSIONS

It is difficult to draw many conclusions from such a small series of cases. However, a larger series is scarcely warranted because of the paucity of findings obtained.

Cholecystography is a safe procedure in pregnancy, and sodium phenoltetraiodophthalein has apparently no effect on the uterus. There were no reactions in this series of cases beyond that which would be anticipated in a like number of women patients. In the early months of pregnancy cholecystography is as valuable in the diagnosis of cholecystic disease as it is in the nonpregnant state. The inconstancy of results of this test of gall bladder function when done in the later stages of gestation, renders it of no practical value for gall bladder diagnosis. Neither race nor the number of pregnancies had any ap-

parent bearing on the observed findings. Cholecystography indicates, at least in the early months of pregnancy, that toxemia does not affect the function of the gall bladder as related to the concentration of the dyes employed. Pregnancy modifies cholecystograms only by shifting the location of the gall bladder. One case in which cholecystography was done both ante- and postpartum indicates the return of the vesicle to its usual position after delivery.

This study suggests that factors other than altered function of the gall bladder are responsible for the high incidence of gallstones in women who have borne children. With the method employed we were unable to demonstrate that there was any stasis of bile. It is possible that hypercholesteremia, normal in pregnancy, either itself or the agencies which bring it about have a part in the development of gallstones. It is possible also that cholelithiasis and cholecystitis in women who have borne children are to be attributed to puerperal infection, which might be so mild as to escape notice. The sequence of events being similar to that demonstrated by Graham[4] in the pathogenesis of cholecystitis: a slight or transient infection, drainage to the liver, the development of a low grade of hepatitis with extension to the gall bladder through the intimate lymphatic arrangement between the two organs. The greater the number of pregnancies, the greater the likelihood of a woman having gallstones; also, the greater the likelihood of a puerperal infection. We feel that these points have never been sufficiently considered.

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SPURIOUS PREGNANCY*

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A CONDITION that presents itself from time to time in the practice of obstetrics is that of spurious pregnancy or pseudocyesis. This condition, characterized by signs and symptoms that frequently simulate very closely the signs and symptoms of pregnancy, may at times give rise to extremely embarrassing situations, both to the physician and to the patient. The study of cases of this nature is very interesting and gives one a rather interesting glimpse of abnormal feminine conduct.

Spurious pregnancy is referred to by a number of terms such as: false pregnancy, phantom pregnancy, imaginary pregnancy, hysterical pregnancy, and simulated pregnancy. Although the term "feigned pregnancy" is used synonymously, its use in this respect is an ill chosen one, since it carries the connotation of malingering, or intentional deception, which is not, strictly speaking, a part of the condition under consideration. The French have coined a term to denote the condition, namely, "grosseuse nerveuse."

The literature on the subject is not very comprehensive. Probably the earliest contributions that have been identified, date from 300 B.C. Hippocrates mentions the condition and one may infer from his writings that observations at that time were rather well grounded on recognized cases in animals as well as in humans. From a rather extensive review of the literature of modern medicine the following facts regarding the published work on the subject are obtained.

Spurious pregnancy has been given considerable attention in the middle of the nineteenth century by such authors as Madden, Montgomery, and Simpson. Of all conditions presented to obstetricians and gynecologists spurious pregnancy has probably excited the least published comment. Most mention of the subject appears in the form of case reports presented at meetings of local medical societies. These cases are reported mainly as interesting examples of abnormal human behavior, or as examples of patients who should have been examined early by the physician in charge. Very few conjectures have been advanced as to the why or as to the wherefore of the condition.

On account of the nature of the condition only a few of the cases are ever seen in hospital practice. Most of the cases are seen in the office or the dispensary where the diagnosis is made before the patient reaches the supposed date of confinement. Horrocks reported a hospital case from Guy's Hospital Reports in 1884. Rosensohn reported ten cases from the antepartum service of the Lying-In Hospital in *Bulletin of Lying-In Hospital* of New York in 1922. These cases were collected over the period of one year, from 1916-1917.

Spurious pregnancy is seen in animals and several references to such cases are made in the literature. These will be considered later. Although no accurate data is at hand to verify the assumption, the condition is probably common to all

*Read at a Meeting of The St. Louis Gynecological Society, April 13, 1928.

races. At least twelve countries are represented in the literature on the subject, and the territory included all continents and was distributed from Scandinavia to South Africa.

It is my experience that in the dispensary more white patients are seen with imaginary pregnancy, than colored, although the colored attendance outnumbers the white by approximately two to one. Practically all of the cases in the literature are reported about white subjects.

There is considerable difference of opinion as to the age at which most cases appear. In most instances recorded, the patients were between 25 and 35 years of age. Simpson states that most cases are seen at the climacteric period. Montgomery thinks that it occurs most frequently at the climacteric period. The reports in the literature do not bear out the latter statement.

As a result of personal observation I believe that most of the cases occur in young individuals who, because of exposure to pregnancy and the undesirability of pregnancy, imagine themselves pregnant. These cases do not present themselves for observation early, on account of the embarrassment attending such visits to the physician, but keep their own council until they are convinced that they are, or are not pregnant. Some of these patients hasten to the sympathetic midwife or the near-by apothecary where the products of imagination may be dispelled as easily as one discards a bit of tissue.

From observations in the dispensary and from reviewing the numerous cases in the literature one may divide the cases into three general types:

First, those women in whom there is a decided fear of pregnancy or an aversion to pregnancy.

Second, women who are extremely desirous of becoming pregnant.

Third, those cases in whom pregnancy is imagined because of some functional disturbance attended by symptoms which simulate the signs or symptoms of pregnancy.

In the first class come the young individuals mentioned above. Many of these are young girls who after illicit intercourse begin to build up a sort of aura of pregnancy. All sorts of emotional conflicts go on. Minor disturbances are interpreted in the light of a prospective pregnancy with its attending shame and uncertain outcome, until the entire organism is thrown out of balance and pseudocyesis is the condition requiring treatment.

In the newly married women similar emotional disturbances often take place, though usually not as marked or as persistent.

In many cases it is extremely difficult to get to the cause of the exciting factors other than the history of some previous illicit intercourse. In two cases, seen in the obstetric dispensary within the past year, the patients were both minors in whom the history of previous

intercourse had no direct connection with the spurious pregnancy, for which they were under observation. Both of these patients had mental ages far below their ages in years.

In making inquiry as to why pregnancy was suspected it was found in each case that on admission of previous intercourse to their mothers, and the development of some presumptive sign of pregnancy, the suggestion was so strongly impressed on the patient, that each girl believed herself actually pregnant and became a full blown case of spurious pregnancy. From the analysis of the social conditions surrounding many of these patients in their homes and places of employment, I believe that many cases are developed from just such surroundings.

A brief outline of one of the cases mentioned above will be of interest here.

F. G., white, aged twenty, single, entered obstetric clinic October 6, 1927. Patient was a rather dull type with the appearance of low mental age. This was subsequently determined as nine to ten years in the neurologic clinic.

Menses started at twelve years and were regular every twenty-eight days with a moderate flow, lasting seven to eight days. Her history, which was subsequently verified, was that on July 3, 1927, she had been forcibly attacked. This attack had been made while she was away from home, against the wishes of her mother. On her return home her mother had become quite abusive and suspected pregnancy at once. The next two menstrual periods became short and scanty, and the following month she did not menstruate. At this time she was sent away from home, and she then became more or less of an outcast.

On admission to the dispensary she was thoroughly convinced of her pregnancy. She complained of nausea and vomiting existing for three weeks, hot flashes, and headaches. Her weight had increased and the abdomen was getting larger. On examination the breasts were found somewhat congested. The abdomen was somewhat enlarged. The uterus could not be felt because of the resistance of the patient and tenderness. Two weeks later examination failed to reveal any further evidence of pregnancy, but it was thought advisable to keep the patient under observation.

For some reason the patient did not return until January 4, 1928. At this time she was still of the opinion that she was pregnant. Nausea was still present though not severe. No menstruation had occurred. The abdomen was larger and the weight had increased 16 pounds since first visit. The uterus was not enlarged. Patient mentioned some indefinite movements in right side which she interpreted as fetal movements. She was told that she was not pregnant but refused to be convinced.

Two weeks later she returned with history of a slight fall a few days before, followed by some pain in side, a few cramps, and a slight bloody discharge on the day of the visit. This discharge had the appearance of a scanty menstrual flow. She was told that this was probably a menstruation and that she likely would menstruate the next month. There had been no increase in the abdomen, and the weight had diminished slightly.

Meanwhile the social condition of the patient had been benefited, and a more satisfactory adjustment of environment had been made. The patient has menstruated normally since and no longer believes herself to be pregnant.

The second type or those who are extremely desirous of becoming pregnant probably present the most extensive picture of spurious pregnancy and are most difficult to convince that their assumptions are wrong. These women are usually older and with their better knowledge of signs and symptoms of pregnancy present a more complete picture of pseudocyesis.

Oftentimes pregnancy in such patients would be of decided advantage from an economic standpoint such as the participation of children in the inheritance of an estate, or in the fixing of an amount of alimony. Often the desire to hold the love of the husband and preserve the marital state is the exciting factor. The condition is noted especially in women who have been married a number of years and are approaching the menopause, without ever having become pregnant.

In two cases that I was able to observe I found that both patients had been married before without issue. In the second marriage both wished to have children, partly because they themselves desired them and partly to convince their husbands that they were not barren. In a number of cases that I have questioned, the fear of sterility seemed to be sufficient to cause the patients to look forward eagerly to any symptom of pregnancy. Probably the greatest exciting factor in spurious pregnancy in this class of patients is the maternal instinct.

It is in this type of case that the condition is most marked and may continue to a later false labor. Many of these patients make rather elaborate preparation for delivery and the reception of the newborn child.

A case under observation a few years ago illustrated many of these features.

M. S., white, aged twenty-seven, gravida i, requested an obstetric examination to determine the duration of a supposed pregnancy. Her previous history was that of irregular menses beginning at fourteen years and remaining irregular until nineteen when some pelvic operation was done. One normal pregnancy six years ago by first husband. Following the pregnancy there was a history of a pelvic inflammatory condition.

Second marriage two years previous to my observation. Patient stated that since her pelvic distress she was afraid that she could never conceive again. Present husband very desirous of children. No contraceptives.

For four or five months she had noted enlargement of abdomen and a gain of 25 pounds in weight. Menses had been very scanty and painful. Nausea had been troublesome almost daily, with vomiting one to two times daily. Patient noted edema of hands and feet. Fetal movements felt for some time by patient. She believed that she was rather near term, four or five weeks.

When I first saw the patient she was making baby clothes. On examination the breasts showed some enlargement. The abdomen was quite large with a very thick panniculus. No abdominal mass was felt; although the patient resisted considerably and seemed to make the abdomen larger. The uterus was only slightly enlarged if at all. There was a small tender mass in the region of the left adnexa. Patient was very much put out on being told that there was no evidence of any

advanced pregnancy. Ten days later, at the regular menstrual time, she had a rather profuse menstruation with some pain. Following this all symptoms disappeared. Since that time she has had two labors at term and one miscarriage.

In the type of patients that have spurious pregnancy associated with some functional disturbance, the cessation of menstruation is probably the most common causative factor. Most of these cases are in women approaching the menopause when emotional reactions are a part of the menopause symptoms. As the periods cease or become scanty, with the increase in weight or enlargement of the abdomen that so many women experience, it is not at all unlikely that the possibility of pregnancy would suggest itself to the woman. This suggestion in the mind of one whose emotions are already in a state of unrest may easily become a child of imagination.

Numerous other disturbances of function may be the exciting factors in the production of spurious pregnancy. Endocrine disorders which have symptoms common to pregnancy sometimes give rise to the picture. Montgomery, and later Madden mention a number of disturbances such as ovarian tumors, ascites, obesity, visceroptosis, and flatus among the exciting factors of the condition. It will be noted that these disturbances occur frequently near the menopause.

It is interesting to note the prevalence of certain signs and symptoms in these cases. Although many cases simulate real pregnancy very closely, it has been pointed out by Montgomery that almost all of them give a history of some phase of the condition that does not follow the normal course of pregnancy. Some may menstruate a number of times after the supposed pregnancy is well advanced. Others may feel life at an unusually early date for a pregnancy. In many cases the long persistence of nausea and vomiting may be quite unusual.

In following through the reported cases a number of signs were studied. As might be expected disturbances of menstruation were the most common disorders. Nearly every case noted had some menstrual disturbance. Nearly every patient missed entirely one period, and over half of the patients did not menstruate as long as the supposed pregnancy existed. The cessation of menses is extremely important to the patient, and as Rosensohn indicates, often is the beginning of a "train of subsequent signs." Not infrequently scant menstruation is the menstrual disturbance encountered.

Changes in the breasts are one of the most frequent signs in instances of imaginary pregnancy. The cases in the literature are not complete enough to tabulate this feature in the symptom complex. In the great majority of cases breast changes were present. About half of these cases showed the presence of some secretion. Increased pigmentation of the areola was observed in a number of instances, but

there is always some reason for doubt about this sign as is also true in regard to vaginal mucosa discoloration.

Nausea and vomiting are present in probably as many as 80 per cent of the cases. Here again there is usually some deviation from the normal course of events. In the early cases, especially those who fear illegitimate pregnancy, nausea and vomiting may occur unusually early and are frequently unusually severe. In a number of instances the nausea and vomiting started before the menstrual period was missed. At times the disturbance becomes so severe that it requires special treatment. In these severe cases, although the gastric disturbance may be a part of some other disorder, the patient is all the more strongly convinced that she is pregnant. This is emphasized in instances where previous pregnancy has been attended by severe gastric disturbances.

Quickening is present in most of the cases in which the imaginary pregnancy lasts five months or longer. It is most frequently observed in the older individuals. This is probably true on account of the disorders that lead these women to imagine pregnancy, such as gas in the intestines, abdominal distention, tumors, and excessive fat deposits. A number of these women give a history of quickening felt long before it would be expected in normal pregnancy. The history of unusually active fetal movements is not at all uncommon.

Although discoloration of the mucous membrane is not always easily distinguished, it appears that in most cases of imaginary pregnancy that have been carefully studied, this sign was absent. Other conditions causing pelvic congestion make this sign a rather doubtful one, as it may be observed in patients who are not pregnant or in whom there is no suspected pregnancy.

In one or two instances of spurious pregnancy abnormalities of pigmentation have been noted. These were probably due to endocrine disturbances, which were responsible for the functional changes that caused the women to believe that pregnancy was present.

On observing a number of histories of imaginary pregnancy, it is noted that in a small number frequency of urination is noted. In some cases this is probably due to the nervousness of the patients, while in others it is due to pressure or irritation by tumors in the abdomen. This is certainly not a frequent symptom.

Practically all of these women suffer from mental and emotional changes. This is a part of the very condition that makes up the picture of spurious pregnancy. Although some women attribute their emotional disturbances to their supposed pregnancy, the imagination of pregnancy itself is the result of some mental reaction. Occasionally the supposition of pregnancy is the outstanding delusion in a psychosis, but these cases are not characteristic of the emotional

changes of spurious pregnancy. Some of the earlier writers regarded pseudocyesis as a monomania.

Some patients do cling to the delusion long after they have been informed that the pregnancy was only mythical. Montgomery cites one case of nine years' duration. Simpson mentions a patient, seen by Dupuytren, in which case the delusion was kept up for fourteen years.

Practically all cases in which the weight was noted showed some increase in weight. This gain was most noticeable in those cases associated with the menopause. In the case of the young woman I mentioned the increase was sixteen pounds over a period of three months.

Enlargement of the abdomen usually accompanies spurious pregnancy. In a number of cases tumors have been apparent to the examining physician. Phantom tumors do not always simulate the gravid uterus. In several instances the phantom tumors have simulated some other intraabdominal masses. The apparent masses have been caused by involuntary or voluntary rigidity of the abdominal wall, thickening of the wall, distention, by gas or fluids, or similar factors. These supposed tumors usually disappear during anesthesia or while the attention of the patient is diverted.

Naturally the positive signs of pregnancy are absent in the condition. Formerly, before modern obstetric procedures were applied to the cases presenting themselves as obstetric patients, errors in diagnosis were common. Palpation of the abdomen in supposed pregnancy would sometimes lead to the impression that fetal movements were present, when only movement of the intestines or gas within the intestines was felt. This phenomenon together with enlargement of the abdomen has confused many medical men, and has in two recorded cases been the determining sign on which laparotomy was performed.

An essay of this nature is scarcely complete without some mention of the termination of these cases. Most of the patients, when told that they are not pregnant, show considerable doubt as to the correctness of the advice of the physician. Many of these women refuse to be convinced that their pregnancy is only imaginary, and will go from one consultant to another repeatedly, apparently never quite convinced of the error of their assumption. Some patients react rather violently to the correct information and will take absurd measures to convince medical attendants that pregnancy is or has been the case. Some will feign a miscarriage as in the cases reported by Pracy, and by Ellsworth. Nielson displays a large number of small bones of birds, that a patient claimed to have passed per rectum in a case of spurious extrauterine pregnancy.

A number of cases of spurious pregnancy go on to spurious labors. When multiparae simulate labor the effect may be very convincing. By virtue of previous experience the regularity of contractions, with

all the attending agony and sounds, may be very successfully imitated. The early literature on the subject graphically describes a number of such labors.

Although the condition has been recognized for centuries, there has been little study given as to its cause. We can easily see why some women should suppose themselves to be pregnant, or why some delusions should include the supposition of pregnancy. It is not so simple, however, to explain the rather definite progression of signs and symptoms that frequently go along to make the spurious pregnancy seem real to the patient and apparent to the observer. I find that in the discussion of most of the reported cases the condition has been ascribed to hysteria. Although the statement is frequently seen that hysteria may simulate almost any condition, it is difficult to explain spurious pregnancy on that basis. A number of these cases do probably represent hysteria, but by no means do all of them do that.

Montgomery who has presented an excellent treatise on simulated pregnancy rather discourages explanation of the condition. Harvey, and later Schmitt, advanced theories which included the supposition of a close relationship between the receptivity of the brain and of the uterus. These theories would indicate that as coitus occurs, there is conceived within the brain the idea of pregnancy which is fostered as the uterus would foster the developing ovum; or "that a woman should be impregnated by the conception of a general immaterial 'idea' and become the artificer of generation."

Hofstaetter emphasizes the disturbance of endocrine function as a probable cause of the condition. Others point out its association with various mental diseases, such as, paranoia, dementia precox, epilepsy, and feeblemindness. None of these mental disturbances, however, represent per se the starting point for spurious pregnancy.

Doerfler attributes the situation to a disturbance of the patient's psyche that leads to the supposition of pregnancy and to the physical changes seen. This may be the key to the situation but for its solution one must go to more fundamental manifestations.

Throughout the lower animal world excellent examples of pseudocyesis have been observed repeatedly. Hippocrates mentioned the condition in lower animals as well as in humans.

Harvey recorded the condition in dogs. Some of these were dogs that had had intercourse without conception following, while others showed the picture without intercourse having taken place. Instances were noted where the actions of the animals simulated the actions of bitches in labor. Examples of similar behavior are frequently noted in fowls where the female has the desire to set but has no eggs to set on.

Haughton was able to produce the picture of phantom pregnancy in the female ass, and to reproduce the condition for verification.

With these instances of animal behavior in mind it is not advisable to limit too closely our presumptions as applied to the humans. It would be rather difficult to attribute phantom pregnancy in the ass to dementia precox; or in the dog to hysteria or paranoid.

Haughton speaks of a feminine attribute, the maternal instinct. Liepmann analyzes phantom pregnancy from a so-called law of the threefold substratum of the female psyche, which he says runs through the entire animal kingdom; namely, inhibition, vulnerability and pansexuality.

It seems that these two writers have certainly indicated the essentials in studying this interesting problem. The thought of a maternal instinct common to all species is certainly a logical deduction. The ancients recognized maternal instinct and the Greeks gave it a name, "storge."

In woman there is that inherent maternal instinct. Her ultimate purpose is to produce offspring. What normal woman is there who does not at some time in her life desire or speculate on having children?

In humans we have the power to think and reason. Primitive to that power lie the instincts. When by artificial restrictions such as the laws of society, physical disability or lack of contact with suitable mates, the instincts are curbed, then an emotional conflict occurs. This emotional conflict goes on between those inherent instincts and the impression one obtains from the inhibiting agency. This does not involve any process of reasoning. As examples of these curbing factors in the case of lower animals, I mention the bars of the cage, the dwarfed animal, or the different genus of the mate, as studied by Haughton.

In the human there are other influences which serve to increase the conflict. Fear, shame, remorse, desire, dislike, and a number of other impressions are founded on reason and experience. When instinct conveys to the female organism the impression that pregnancy is probable, or should be the case, then the entire organism undergoes a reaction. Thoughts of pregnancy are evolved concerning the possibility of pregnancy and the consequences resulting from that condition. These thoughts are increased by desire or dread of pregnancy, or by some functional disturbance denoting that pregnancy is probable.

There is then, on the one hand, instinct calling for pregnancy with an attempt to simulate reactions common to pregnancy. On the other hand, we have conclusions formed as a result of thoughts on the subject.

If these conclusions coincide with the promptings of instinct, the picture of pregnancy results. This picture becomes more and more fixed in the mind of the patient giving rise to a chain of signs and symptoms brought about by emotional disturbances. This continues until stronger conclusions to the contrary are derived, being induced

by the conclusions of the examining consultant, or as a result of physical manifestations ruling against pregnancy.

If on the contrary the mental conclusions are negative to the proposition presented by instinct, then the woman dismisses the possibility and looks elsewhere for the source of functional disturbances, if any are present.

I believe that the conclusions that I have just presented in regard to spurious pregnancy will apply to almost all cases of the condition. These conclusions also seem to explain the greater frequency of the condition in women of limited mental capacity, which fact I believe is true, from cases studied in the literature and from cases coming under my own observation. The relation between emotional disturbances and functional disturbances I have not attempted to explain. Possibly an understanding of this phase would give us a better key to the situation.

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RADIATION THERAPY IN GYNECOLOGY*

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SINCE the advent of radiation therapy, gynecology has offered a most fertile field for its employment in the treatment of women's ills. My object is to present an outline of the work that for the past three years has been carried on with a gratifying measure of success by the Radiation Therapy service of the largest public general hospital of the metropolis. It is only three years ago that at the instance of Dr. Frederick C. Holden, radiation therapy in gynecologic conditions was made available to patients on his service at Bellevue. During this comparatively brief time we have been able to work out a few definite ideas as to the advisability of its use in gynecology. As employed by us, radiation therapy makes use of the radiant energy of x-rays, radium, and the high frequency current.

As a normal routine, all cases are divided into two main groups, those which have benign and those which have malignant lesions. While the same modalities are used in both groups, the method of procedure and employment varies according to the condition of the patient, and as to whether the lesion is malignant or nonmalignant, and if malignant, whether primary or a recurrent lesion.

Bellevue, being a general municipal hospital, receives all kinds and types of gynecologic patients. At the first examining post of the gynecologic service, it is decided whether or not the patient requires hospitalization. It has been found that but a few conditions can be treated with radiation therapy in an ambulatory manner, the vast majority of cases referred for radiation must be hospitalized.

In that very large group of patients suffering from benign conditions, surgical procedure is usually the method of choice. However, even in the benign cases, radiation can be properly employed, as for example, where the patient is a poor surgical risk, or where surgery has been attempted and failed, or where other medical or social reasons oppose surgical interference.

In the malignancies of the pelvis, radiation has shown such unmistakably good results, that its use in these conditions has now become quite a routine procedure. At Bellevue, malignancy of the cervix is in fact no longer regarded a surgical condition, and in this type of lesion the entire brunt of treatment is borne by radiation alone. In many of the other pelvic lesions, radiation shares equally with surgery in the attempt to control the condition, while in numer-

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ous instances it is relied upon to counteract the dissemination of disease engendered by previous surgical interference.

It is not our province, however, to allocate precisely where and when radiation should replace surgical therapy. Our policy has been rather to cooperate fully and freely with the gynecologist in order that the patient may reap the benefit of our combined study and service. Frequently the pathologic picture presented required special study, and tissue analysis was done in all cases where possible. Our association with the gynecologic and pathologic services has been a most happy one, and in Drs. Holden and Symmers, we have found an unusually fine spirit of open minded cooperation.

During the period of 1925 to 1927, 255 gynecologic cases were treated with radiation. Of these, 111 were malignant and 144 were benign.

In the benign group, the conditions treated were:

1. Newgrowths in the pelvis: (a) myoma uteri; (b) benign growths of the vulva and vagina; (c) urethral carunele.
2. Functional conditions: (a) amenorrhea; (b) dysmenorrhea; (c) metrorrhagia.
3. Dermatologic conditions: (a) eczema; (b) pruritus.
4. Inflammatory conditions of the (a) adnexa and (b) joints.
5. Tuberculosis of (a) peritoneum; (b) adnexa; (c) cervix.

The following malignant conditions have been treated: carcinoma of the vulva, vagina, urethra, cervix, uterus, adnexa, and ovary; sarcoma of the ovary, uterus, and cervix; myxosarcoma; metastatic foci.

As has been shown, therefore, a great many conditions are treated with highly gratifying results by radiation. This form of therapy, however, is not offered as a universal panacea for the cure of all gynecologic diseases, but, where judiciously and properly employed, it offers a form of therapy which either alone or as an adjunct to surgery, very often relieves conditions in which all other forms of therapy have failed.

In general, then, what can radiation offer in the way of therapy? What type of radiation should be utilized in a given condition, and finally, what are the contraindications to its use? To answer briefly, radiation when properly used can cure certain conditions, it can ameliorate the severity of others, it can help to render operable some conditions which might otherwise be classed as inoperable, and finally act as a palliative in advanced malignancies.

The type of modality to be used in any given case varies with the type, location, histology, and extent of the lesion; e.g., in malignancy of the ovary or of the body of the uterus where surgical removal is still feasible, surgery is first employed, followed by radiation. As a general rule, large deep-seated lesions with or without disseminated

metastases, are treated by high voltage x-rays, while localized lesions or those easily gotten at from surface openings are treated with radium. Inflammatory lesions are treated by x-rays. Medical diathermy is indicated in chronic adnexal infections and in the painful lesions of pelvis and back of idiopathic origin. In the treatment of cervical malignancies, a combination of x-rays and radium is employed. Large bulky tumors are first treated by removal of the mass, preferably by surgical endothermy, then radiated.

Regarding medical diathermy, we began using this method of therapy only a short time ago, but the results obtained warrant our continuing its use. In those cases where there is a persistent adnexal involvement, with board-like abdomen, tenderness and no discharge, we have found that small repeated daily doses of moderate diathermic heat to the pelvis have given many good results. The hard frozen pelvis has softened down, the exudate has been absorbed and in some cases the pus has been centered to an easily drained area. Often a nondraining sinus to a supposed pus pocket is made to drain by diathermy.

Some really gratifying results have been achieved by its judicious use in idiopathic pains of the back, and in those painful postoperative pelvic cases which defy all sorts of other therapy. Diathermy is not a cure-all, nor is it indicated in all cases, but when properly used does give results that are gratifying to the patient and doctor.

The application of radium is contraindicated in infectious lesions, it is always a surgical procedure, and the rules for proper surgical manipulation apply to its use as well. X-ray treatment, on the other hand, can be given to an ambulatory patient, it does not require keeping the patient in bed and is not contraindicated in infectious conditions, except in rare instances.

In the matter of transfusions, we believe they enhance the value of radiation therapy in all cases where body resistance is lowered. The same rules governing the reasons for transfusions in other medical or surgical conditions apply equally well in connection with radiation therapy. If possible, transfusion should be given in all cases of malignancy before radiation treatment is carried out. Transfusions in addition to general body hygiene and building up of the patient's strength materially aid recuperation.

Specifically, radiation may destroy tissue or merely inhibit its growth or action, on the other hand it may stimulate tissue growth or action. When used in mild doses, radiation causes a response which is interpreted as being a stimulation reaction of body tissue; when used in severe dosage, the tissue or its functional reactions are more or less completely destroyed. The proper use of radiation nicely harmonizes these known reactions with the expected therapeutic results.

SUMMARY

The x-rays are used generally in all benign and tuberculous lesions, in functional disturbances, in metastatic and widespread malignant conditions, as a postoperative aid to surgery in malignant conditions, and finally in such cases where only a palliative effect can be hoped for.

High voltage x-rays yield excellent results in fibroids, excepting the submucous type, and in functional disturbances such as amenorrhea, sterility, and dysmenorrhea.

Among the patients we see at Bellevue, amenorrhea is not a condition for which relief is sought; it is but part of the symptom complex. We have treated thirteen patients, of these 6 were married and 7 were single. The oldest was thirty, the youngest seventeen years old. The shortest period of amenorrhea was two, the longest period twenty-five months.

Results: menstruated, 9 or 69 per cent; failed to menstruate, none; unknown results, 4 or 21 per cent.

In metrorrhagias of specific or idiopathic origin where surgery is contraindicated, high voltage x-rays usually bring prompt relief. In fibroid uterine lesions we consider radiation indicated when surgical interference is contraindicated, when the childbearing period is past, when the patient refuses operation, or when sterilization is required for other associated lesions. Our belief is that the size and condition of the tumor have no bearing on the question of the feasibility of radiation.

The total number of fibroid cases treated was 60, the youngest patient being twenty-four, and the oldest seventy-three years old.

Ages: 20 between twenty-four and twenty-nine years; 29 between forty and forty-six; 7 between forty-seven and fifty-nine; and 1 between sixty and seventy-three years. Age not given in three cases.

Of these 60 patients, 12 were single, 39 were married, and 9 were widows.

Infection was present in 9 cases or 15 per cent; not present in 51 cases or 85 per cent.

Twenty-two, or 37 per cent, had no children; 10, or 16 per cent, had one; 25, or 42 per cent, more than one child. Concerning 3, or 5 per cent, no information available.

Ten, or 16 per cent, had one; 16, or 27 per cent, several; and 34, or 57 per cent, had no miscarriage.

Symptoms recorded: bleeding in 44, or 57 per cent; of these excessive bleeding in 18, or 30 per cent; palpable tumor mass in 41; tumor at umbilicus or above in 1, fairly large, 18; no tumor palpable in 19, or 32 per cent, of cases, probably submucous tumor in 1.

Treatment: x-rays alone, 57; radium alone, 6; x-rays and radium, 2; operation following x-rays, 3; operation following x-rays and radium, 2.

Results: bleeding stopped, 39, or 65 per cent; failures, 4, or 7 per cent; unknown results, 17, or 28 per cent.

Failures: death following x-rays, none; death following x-rays and radium, 1; failure by x-rays alone, 3, or 5 per cent; failure by x-rays and radium, 2, or 3 per cent.

Regarding therapeutic abortions by the x-rays, we have been successful in only three cases out of nine so treated.

In tuberculous lesions of the pelvis, x-rays give prompt relief, and in those cases of persistent sinus often cure the condition. In tuberculosis of the cervix, radium therapy is the method of choice.

In malignancy of the cervix, the type and histology of the lesion determine the particular method of procedure and the result. The more adult the type of tumor tissue, the more involved the lesion is, and the less it reacts to radiation, and therefore the more malignant the condition.

In the 72 treated cases in our series, 2 cases were early operable, 70 were inoperable, advanced. Of these 11 cases were recurrences, following previous operations or radiations. In all cases radiation was preceded by hygienic treatment through nourishing feeding and daily bowel and vaginal cleansing.

Radiation was given by x-rays and radium, and in five cases, the large cervix tumor mass was first removed by endothermy.

The details of the cases treated are as follows: Of these 72 patients 59, or 82 per cent, were white and 13, or 18 per cent, colored. Fifty-one were married, none single, and 21 widowed.

The youngest was twenty-six, the oldest eighty-four years old. The ages ranging between twenty-six and thirty in 5; thirty-one and forty in 20; forty-one and fifty in 29; fifty-one and sixty in 16; sixty-one and eighty-four in 5 cases.

Three, or 4 per cent, had no children; 15, or 21 per cent, one child, and 54, or 75 per cent, two or more children.

There were noted: miscarriages, in 29, or 40 per cent; normal labor in 63, or 87 per cent; difficult labor in 6, or 8 per cent.

The condition was found operable in 2, or 3 per cent; inoperable in 70, or 97 per cent.

Previous treatment was noted in 25, or 35 per cent, and previous operation in 22: 9 hysterectomies, 2 cervix amputations, and 11 other gynecologic operations.

Previous radiation was recorded in 3 and no previous treatment in 47, or 65 per cent, of the cases.

The stage of disease was as follows: primary, 61, or 84 per cent; recurrence, 11, or 16 per cent; following operation, 10; following previous radiation, 1.

Condition of lesion: limited to cervix in 2, or 3 per cent; parametrial involvement in 70, or 97 per cent; excavated lesion, in 6, or

8 per cent; hypertrophied or cauliflower type in 6, or 8 per cent, accompanied by vaginal involvement in 7, or 9 per cent.

Histology: basal cell in 2, or 3 per cent; squamous cell in 14, or 19 per cent; plexiform in 33, or 46 per cent; adenocarcinoma in 10, or 14 per cent; undifferentiated in 13, or 18 per cent.

Wassermanns were found: positive in 6, or 8 per cent; negative in 56, or 78 per cent, and unknown in 10, or 14 per cent.

Treatment consisted in: x-ray alone in 14; radium alone in 3; x-ray and radium in 49; and endothermy, x-ray and radium in 5.

Results: known dead, 12, or 16 per cent; known living, 40, or 56 per cent; unknown, 20, or 28 per cent.

Analysis of death: occurred following treatment in 1 case; occurred five, seven, nine, ten, twelve, and fourteen months after treatment in 1 case each; thirteen months after treatment in 2 cases, and 17 months after treatment in 3 cases.

Causes of death: uremia, in 1 case; asthenia and cachexia in 10 cases; advancement of disease with terminal hemorrhage in 1 case.

Histology of the lesion of the 12 known dead: plexiform epithelioma in 8 cases; squamous-cell epithelioma in 2 cases; and adenocarcinoma in 2 cases.

In conclusion, radiation is a really helpful means of treating many gynecologic conditions. It is not a panacea for all lesions, nor is it the method of choice in the treatment of all conditions, but when properly, judiciously and carefully used, radiation is a potent factor in the care of the gynecologic patient.

The radiation therapist and the gynecologist must cooperate, and surgical judgment must be followed in deciding the course of treatment.

The rôle of radiation therapist is not an easy one in the family of medical specialists, but if he will constantly cooperate with the gynecologist, and treat each case as an individual entity, using the judgment of his colleague with regard to the course of treatment to be pursued, the results that will be obtained will prove highly gratifying to all concerned.

55 East Eighty-Sixth Street.

GONOCOCCUS INFECTION IN FEMALE CHILDREN

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GONOCOCCUS infection of the genital organs in infants and young girls is a condition which concerns the general practitioner and the gynecologist, as well as the pediatrician, to whom it presents an ever present menace. The innocence of the acquired infection, the difficulties encountered in diagnosis, the necessity for prolonged treatment, the practical impossibility of pronouncing a patient cured, and the frequency of recurrences are phases of the disease which justify any contribution concerned with pathology, diagnosis, or treatment. We have studied 42 cases of definite gonococcal vulvovaginitis, which have come under the care of the department during the past two years. In each patient the gonococci were demonstrated in the secretions either at the time of admission or subsequently.

AGE INCIDENCE

The average age of the patients was six and one-half years, the oldest child being twelve years and the youngest nine months.

SOURCE OF INFECTION

In the majority of these cases we have been unable to determine the probable etiology with any definiteness, although in 13 patients where the history was quite clear cut, it was indicated that contamination from other infected members of the family played the greatest rôle, since in four cases the father, in two the mother, and in one an older sister were known to have had the disease. Two other patients apparently contracted the disease from playmates who were known to have had a vaginal discharge; in three of the older children rape was indicated, and one child became infected during an epidemic in a Children's Home. It is worthy of note that when one child becomes infected, the other female children in the family usually contract the disease, unless effective isolation is practiced. We have noted three such families where all the female children were under treatment. It might possibly be assumed that in the older children attempted intercourse was a factor, although direct evidence is lacking. In no instance was the disease contracted by direct contact with an infected mother at the time of birth. It may be that children born of gonorrheal mothers have an immunity which protects them for some time and explains why even in a large venereal obstetric clinic infection at the time of birth is rarely noted.

DIAGNOSIS

We still feel that the most reliable method of diagnosis is the close correlation of the physical findings with a careful examination of smears stained with the Gram method. Burke's[1] modification of the original Gram stain is most satisfactory. Positive findings are usually easily made when the disease is recent but become more difficult as the infection becomes chronic. Our experience with diagnostic cultures agrees very closely with that of Stein,[2, 3] that they cannot be relied upon. We have never obtained a positive culture where the smear examination was negative, but in approximately one-half the cases with positive smears, we have been unable to grow the organism. We have had no personal experience with the complement fixation or with the skin test.

METHOD OF EXAMINATION

As early as 1893, Koplick[4] expressed the opinion that the vagina was the seat of the infection but that involvement of the cervix was frequently present and explained the intractable nature of the disease. Scommazoni[5] and Hess[6, 7], who have had opportunities to study under the microscope the cervices of children who had died from intercurrent diseases have reported evidences of cervical inflammation. In 1924, Randall,[8] from this clinic, reported 11 children with vulvovaginitis which was resistant to the ordinary methods of treatment, and in 5 of whom examination with the vaginoscope revealed the presence of cervical disease.

With these facts in mind, our routine demands examination of the cervix through an electrically lighted, Koch, eight-centimeter urethroscope of appropriate size (22 to 26, French). A short instrument is preferable, since the manipulations incident to obtaining smears and giving treatments are more easily carried out than when longer instruments are used. As a rule, the instrument can be passed through the hymenal orifice without difficulty, but occasionally incision of the hymen may be necessary. With the child on the edge of the table and with the hips elevated, the urethroscope is passed into the vagina and a careful inspection made. Usually the cervix as well as the vaginal walls are reddened, while occasionally small punctate hemorrhagic areas are visible, and frequently a drop of pus protrudes from the external os. After the cervix has been cleansed with a small piece of cotton on the end of a nasal applicator, a fine platinum loop is passed into the cervical canal and material obtained for smear examination. The smear is prepared by tapping the loop gently into a small drop of distilled water on the slide. Other smears are taken from the vagina, vulva, and urethra as indicated, and more recently also from the rectum.

FINDINGS

Of the 42 cases thus examined at the time of admission, 40, or 95 per cent, showed gonococci in the cervical smears before we had instituted any treatment. Approximately one-half of the cases had had

treatments elsewhere, leaving 20 children with gonococci in the cervix before any treatment had been given. In the patients who had been treated, there is the possibility that vaginal irrigations had washed the organisms into the cervical canal, but in 20 of the cases this cannot be argued, since there had been no treatment.

It seems logical that the cervical involvement would occur chiefly in the chronic form of the disease, but our experience would indicate that it is also present in the early stages of the infection. Two of our patients had contracted the infection only two weeks before admission, and had been brought to the hospital very shortly after the appearance of the discharge, while another case was of not more than three weeks' duration. In none of these children had there been any previous manipulations or irrigations, but the smears from the cervix showed gonococci.

The organisms were obtained in smears from the urethra in only 9 of the cases, or 21 per cent, the ages of the children varying from six to eleven years.

Although Fraser[9, 10] reports having found the organisms in the rectums in 59 of 63 cases, we have been unable to demonstrate them in any of a considerable number of our more recent admissions. Tod[11] apparently has had a similar experience.

COMPLICATIONS

None of the more usual complications of gonorrhea as seen in the adult female, salpingitis, peritonitis, arthritis, or ophthalmia were observed in this series, although there are many such cases recorded in literature. We consider the cervicitis an almost constant finding, and as such do not consider it a complication.

TREATMENT

It is generally recognized that hygienic measures, including a daily bath and frequent cleansing of the vulva, are important in the treatment of gonorrhea in the female child, but there is as yet no uniformity of opinion as to the germicide which is most efficacious. Our routine treatment includes twice-daily, hot, vaginal douches with saline solution. Immediately after the morning douche, the cervix is exposed through a urethroscope and a gonococcicide applied to the cervical canal by means of a nasal applicator. The portio and the vaginal vaults are painted thoroughly, and the lower vaginal walls are treated as the instrument is withdrawn slowly. The same antiseptic is applied to the vestibule and vulva, and a few drops are instilled into the urethra.

In a clinical test to establish for ourselves the relative efficacy of various methods of treatment, we compared the time required for smears to become negative and to remain negative for three consecutive weeks under treatment and for an additional week without treat-

ment. Smears were taken weekly, all treatment being omitted on the day preceding this examination. As shown in Table I, 5 per cent mercurochrome was the most effective of the remedies we tried.

TABLE I. RESULTS WITH VARIOUS ANTISEPTICS

DRUG	AVERAGE NUMBER OF WEEKS FOR SMEARS TO BECOME NEGATIVE
Mercurochrome, 5 per cent	2½
Mercurochrome, 2 per cent	4
Mercurochrome ointment, 2 per cent	5½
Argyrol, 40 per cent	7½

After prolonged treatment with one antiseptic with no apparent effect, a change to another drug will frequently clear up the discharge in a relatively short time and render the secretions gonococcus-free. A weak, saline douche seems more satisfactory than either potassium permanganate, lactic acid, or plain water. Our experience suggests that in addition to reducing the local inflammation and the discharge, such a douche is of some value in shortening the course of the disease.

At one time, thinking that perhaps gonorrhea was after all a strictly self-limiting disease, we observed several cases for some weeks without any treatment other than ordinary cleanliness. There was, under such conditions, no apparent improvement in the local condition and the discharge continued to show gonococci.

No consistent relation was found between the duration of the disease and its response to treatment, although in general the more recent infections required a longer time for complete disappearance of the organisms from the secretions.

We have not as yet given vaccines a satisfactory trial, but the reports in the literature are very contradictory, Hamilton,[12] Condat,[13] and Blanco and Villazon[14] reporting good results, while Barnett[15] could detect no definite improvement when vaccines were relied upon. We have tried "Gonalin," a commercial preparation of killed gonococci, with no noteworthy results.

STANDARDS OF CURE

It is practically impossible to state whether a patient is cured, since recurrences are so common. We have arbitrarily adopted, as a working standard, three consecutive weekly smears during which time treatment is continued, followed by a week of observation without treatment. If at the end of this period, the smears are still negative, the patient is discharged as "noninfectious" but the parents are instructed to have gynecologic and smear examinations made at the end of six weeks, six months, and one year.

RECURRENCES

Valentine[16] suggests that relapse occurs in almost all cases, while Fraser[9] states that only three of his cases relapsed, although three

others did not benefit from the treatment, and Norris and Mickelberg[17] give the frequency of recurrences as 12 per cent. The incidence of relapse will undoubtedly vary with the standard of cure. In our 42 cases with observations varying from three months to two years, there were 7 patients who had relapses (16 per cent). Of these 7, one had three and another two recurrences, making our total incidence of relapse 23 per cent. In certain instances, so-called relapses are really reinfections, but in the majority this factor can be well eliminated and a diagnosis of true recurrence must be made.

PERIOD OF HOSPITALIZATION

In this series, and with the various methods of treatment used, the average time necessary for smears to become negative was four weeks (longest, seventeen weeks; and shortest, one week), and the average number of days in the hospital after the smears were negative and before the patient was discharged according to our standards of probable cure, was thirty-four days. This made the average period of hospitalization about nine weeks.

SIMILARITY TO GONORRHEA IN ADULT FEMALES

Pearce,[18] by immunologic tests, attempted to divide the gonococcus group of organisms into infantile and adult types, assuming the former to be the causative organisms in vulvovaginitis. Clinically, such a differentiation has never been supported since many of the cases are acquired from adult members of the family, and to assume that the organism causing the vulvovaginitis is different from the organism causing gonorrhea in the adult, from whom it was acquired, seems unreasonable. Torrey and Buckell[19] have concluded from more recent serologic studies that "cross absorption experiments indicate that no definite serologic distinction may be drawn between strains isolated from vulvovaginitis cases and those from gonococcus infections in adults."

Our experience indicates that the only real differences between the disease in infants and in adults are the mode of acquiring the infection and the frequency of urethritis and salpingitis. We know of no definite reason for the relative infrequency of urethritis, although it is interesting that none of our very young children had organisms in the urethra, the youngest being six years of age. The small, undeveloped labia, the absence of pubic hair, and the young type of epithelium are the usual explanations for the ease with which the disease may be acquired by children; while the relative infrequency of salpingitis can surely be explained by the absence of menstruation, since the upward spread of the infection in adults most frequently occurs in association with that function.

The results of treatment are hardly more satisfactory in the adult female than in the child, even though here we may resort to the use

of the electric cautery and diathermy, methods which are not recommended in children. The problem of recurrence is similar, although in the adult it becomes increasingly difficult to rule out reinfection.

We are, therefore, forced to conclude that there is a marked similarity between the disease in the infant and in the adult, and suggest that the disease is better described by the term gonococcus infection in female children rather than gonococcus vulvovaginitis, which does not describe the full extent of the pathologic involvement.

SUMMARY

Contamination from some member of the family was, in this series, the most frequent source of gonococcus infection in female children, although in the majority of cases no etiologic history could be obtained.

The most reliable method of diagnosis consists in a correlation between the clinical findings and the results of a Gram stain of the secretions.

Smears from the cervical canal were positive for the gonococcus in 40 of 42 cases.

There was no definite relation between the duration of the infection and the cervical involvement. Even in recent cases gonococci were found in the cervix.

Gonococci were obtained from the urethra in nine cases, or 21 per cent, but never in children under six years of age.

Mercurochrome (5 per cent) caused the organisms to disappear from the secretions more quickly than either 2 per cent mercurochrome solution, 2 per cent mercurochrome ointment, or 40 per cent argyrol.

Four weeks was the average time necessary to procure negative smears.

Relapse occurred in approximately 23 per cent of the cases.

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PRESERVATION OF OVARY BY MEANS OF INTRAUTERINE TRANSPLANTATION IN RADICAL OPERATIONS FOR ADNEXAL DISEASE*

By O. S. Pavlik, Ph.G., M.D., F.A.C.S., Chicago, Illinois

IN NO other field of surgery is function so light-heartedly sacrificed and with such disastrous results as in the inflammatory diseases of the female generative organs. The gynecologists of the past and a good many of the present day still cling to the old formula of making "a clean sweep" in gonorrheal and other forms of inflammation of tubes and ovaries. The abrupt climacteric disturbances are obvious, but who can follow the more subtle effects of loss of ovarian function, the break in the balance of endocrine secretions and of premature senility? We shudder to think that the price of gonorrheal infection in the male would be castration.

The trend of modern surgery is distinctly toward preservation of function. We are not so much concerned with our ability to remove an organ, as with the question of how the function of the organism will be affected thereby.

Attempts at preservation of ovarian function in mutilating operations upon female generative organs have occupied the minds of gynecologists for some time. An admirable review of the literature on the subject was presented by Dr. F. H. Martin.[1] Pieces of ovary were transplanted into the anterior sheaths of the rectus muscle, into the space between its posterior sheath and the peritoneum, and into the broad ligament, in these cases. Ovarian function could be preserved for variable periods of time. The first attempt to preserve the possibility of pregnancy was made by Robert Morris[2] in 1895. He implanted the healthy portion of a supposedly diseased ovary into the interior of the stump of one oviduct, after radical removal of both tubes and ovaries. The patient became pregnant one month later but aborted at the end of two months.

The report of individual cases and of small series by different authors may be omitted, as this work has already been done by W. L. Estes, Jr.,[3, 4] by Marian Douglas and others. I shall call your attention here to two fairly large series, that of W. L. Estes of Bethlehem, Pennsylvania, and of Theophille Tuffier of Paris.

Briefly, the technic employed by W. L. Estes, Sr., and Jr., is as follows: "The tube of the implanted site is removed, together with enough of the horn of the uterus at the tubal attachment to leave a raw area the size of the cut surface of the ovary. In the center of this surface will be seen the opening into the uterine cavity less than one-quarter of a centimeter in diameter. A longitudinal slice is

*From the services of the Cook County and Wesley Memorial Hospitals.
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taken through the full diameter of the ovary, removing usually about one-quarter of it from the surface opposite its ligament and mesentery. The amount of ovary removed depends upon the amount of cystic degeneration or inflammation that may be present. The cut surface of the ovary is then turned over upon the denuded area of the uterine horn and sutured in place by a continuous catgut suture. The round ligament is then plicated over this entire area by suture to the uterus, to cover and completely peritonealize it.'' By this technic they have operated upon one hundred patients, but were able to follow up only twenty-seven of these. Pregnancy occurred in four, or fifteen per cent. Two patients aborted at about the third month while two went on to full term. The full-term children are living and normal. Menses were regular in nineteen, irregular in four. One patient only failed to menstruate. Three had to be reoperated upon because of discomfort, pain, and disability. A cystic enlargement of the implanted ovary was found in two. Estes makes this conclusion: ''If pregnancy occurs after implantation, it must be because the surface of a graafian follicle comes in contact with the opening of the tube and heals in this position, so that when the follicle ruptures, the ovum can enter the uterus. Therefore, as the graafian follicles are in the cortex, a higher percentage of pregnancies may follow the operation, if care is taken to remove either a thin layer of the surface or fully seven-eighths of the entire ovary, so that ovary is sectioned through the cortex and a cut section of cortex with follicles is implanted upon the uterus and tubal opening.''

Tuffier's[5, 6] series includes twenty-nine observed cases. His method of operating was as follows: The uterine cavity is dilated by means of tents, twenty-four hours before the operation. He makes a lateral posterior incision through the uterine wall, into the cavity, and introduces the ovary into the uterus so that its head is in the cavity and its neck is in the uterine musculature. In that way the ovary is prevented from hanging like a polyp. He did not have a single mortality. Results were excellent in twenty-one cases. None of his cases became pregnant. He mentions, however Petit's case in which the woman became pregnant and was delivered at full term. As a result of his experience Tuffier states that trans position of the ovary, with or without the pedicle, exerted a very favorable action upon the general condition of the women. Menses appeared from three to five months after operation and persisted for periods varying from five to ten years, in some without a break. The operation may be followed by pregnancy with normal birth. The only complication noted was mild pain, preceding menstruation, in about fifty per cent of cases.

Marion Douglas[7] had one pregnancy in a series of four cases. This pregnancy terminated at the tenth week. The case of W. S. Bainbridge[8] is quite interesting. He operated in 1905, upon a patient with severe suppurative condition of both tubes and ovaries. He implanted a small piece of ovary into the uterine horn. Four months later the patient menstruated and one and one-half years later she was delivered of a normal, full-term child. A year later the husband died. Menstrual life was quite regular and normal. Menopause took place at fifty-one years, twelve years after the operation.

I wish now to present a series of sixteen patients operated upon by myself at the Wesley Memorial and the Cook County Hospitals. In a group of eleven cases a free transplant of a piece of ovary was made into the uterine horn. In the second group of five cases, the ovary was transplanted into the uterine horn according to the method of Estes with its vascular pedicle preserved. Operations were performed for inflammatory and suppurative diseases of tubes and ovaries. Follow-up study was very difficult because of the nature of the mate-

rial. All eleven women began to menstruate six weeks to three months after the operation. No pregnancy occurred. Two had positive Wassermann reactions. Miscarriages were common in the previous history. The only complication noted was slight premenstrual cramps in certain cases which were followed for from six months to two years. Menstruation continued uninterrupted in all.

In the second group of cases, five women were operated upon. In all five, menstruation began three weeks to two months after the operation. One became pregnant. Her history is as follows: In the early part of 1924, the patient had had the appendix removed and both tubes ligated because she did not wish children. She was now desirous of pregnancy. The right ovary was implanted into the uterine horn. She menstruated two months later and every month thereafter. She did not have any pain and the amount of flow was about normal. She presented herself for examination nine months later, stating that she had missed the last two periods. Examination showed the uterus enlarged to about the size of a two months' pregnancy; there was marked tenderness in the region of the right ovary. Two days later she began to flow, and four days later she expelled uterine contents which on examination, proved to be a product of a two months' conception. Menstruation commenced one month later and continued regularly.

SUMMARY

The type of cases which come to the service of Cook County Hospital makes "a follow-up" exceedingly difficult for a period sufficiently long. Frequency of syphilis makes the possibility of pregnancy rather remote. Of sixteen cases of transplantation all resumed menstrual function from three weeks to three months after the operation. Slight dysmenorrhea was the only complication noted in some of the cases. Out of a group of five cases of transplantation with preservation of the pedicle, all menstruated and one became pregnant six months later, but aborted at two months. The effect of operation upon the health and the psychic states of the women was most gratifying. My experience coincides with that of Estes and Tuffier. Preservation of ovarian function in these cases is a distinct advance over the older castrating procedures.

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(For discussion, see page 896.)

VAGINAL DISCHARGE DUE TO TRICHOMONAS VAGINALIS*

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IN CERTAIN patients with a persistent vaginal discharge which is very difficult to cure, smears made of the vaginal and cervical discharge (and urethral if any is present) fail to detect the causative organism. When gonococci are found, they are usually assumed to be responsible for the discharge. In many instances, no pathogenic organism is found on stained slides. The organism known as the Trichomonas vaginalis, which is a parasitic, flagellated, protozoon and causes a characteristic vaginal discharge to be described in this paper, is nearly always overlooked because it is impossible to detect in stained preparations unless one has special information concerning its characteristics. It is, however, very easily found in a hanging drop. Unfortunately a hanging drop examination is seldom made of a vaginal discharge although such an examination should be a routine one as a preliminary to the treatment of every discharge.

The Trichomonas vaginalis was first described by Donné in 1837. Hausmann in 1870 reported that he had found this organism in the vaginas of 37 per cent of pregnant and in 40 per cent of nonpregnant women. The most important clinical work on this protozoon was done by Hoehne, who at the time of his report in 1916 had treated more than 100 patients. In a large series of routine examinations of vaginal secretions and discharges, Hoehne found the organism in 34 per cent of pregnant and in 28 per cent of nonpregnant women, but in most cases the number of organisms was small. Reuling found the parasite in 18.4 per cent of women, and Schmid and Kamniker in 69.9 per cent. All these reports came from Germany but the organism has been found in other parts of the world as evidenced by the fact that Ponoschina found it in 30 per cent of adult women in Russia, Brumpt observed it in 10 per cent of women in a Parisian gynecologic clinic, and Hegner found it in 50 per cent of 32 women examined in Honduras and Costa Rica.

The pathogenicity of the Trichomonas vaginalis has not been definitely proved, hence, the matter is still one of dispute. Hoehne, like Donné, Hausmann and Kölliker and Scanzoni, found that the trichomonas was present only in women in whom the vaginal secretion was abnormal. In most instances there was an excessive number of leucocytes. Marchand and also Arnold says the organism does not cause disease but it exists on a pathologically changed vaginal mucosa. Hoehne, Gragert, Liss, Traugott, Littauer, Schmid and Kamniker and A. Seitz claim that the organism is distinctly pathogenic in many cases, whereas Löser, Wolfring, Füth, Neumann, Mayer and Seeliger maintain that the parasite is harmless.

In the vaginas of pregnant women Hausmann found this flagellate in 37 per cent, Hoehne in 34 per cent, Schmid and Kamniker in 24.4 per cent, Seitz in 20

*Read before the Chicago Gynecological Society, February 18, 1928.

per cent and Liss in 19.5 per cent. Nearly all of Schmid and Kamniker's patients had fever in the puerperium, especially those who had had lacerations or operative deliveries. Hence, according to these authors, the presence of trichomonas during pregnancy forbodes a febrile puerperium. Gragert as well as Liss came to the same conclusion and urges treatment during pregnancy and the avoidance of internal examinations and manipulations during labor.

The origin of the Trichomonas vaginalis is unsettled. A trichomonas organism is frequently encountered in the mouth and in the feces of normal persons. Bensen, and also Webster, believes the Trichomonas vaginalis is identical with the trichomonas found in the mouth and in the intestines. Lynch, however, says these three organisms have not been certainly identified as the same.

The best way to study the organism is by means of hanging drop preparations, or by diluting a drop of vaginal secretion with a drop

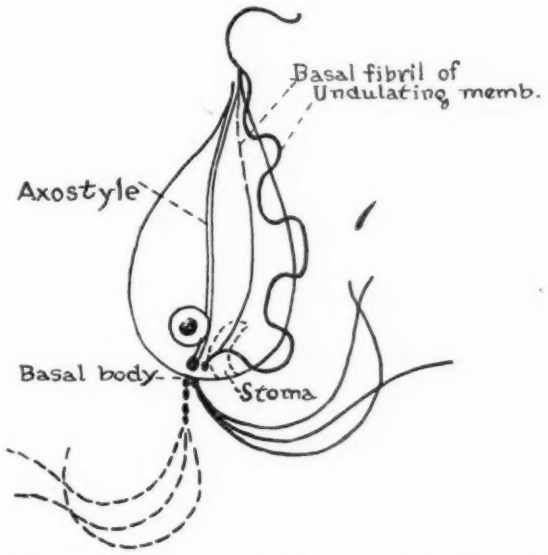

Fig. 1.—Shows essential structures of the Trichomonas vaginalis. (From Rodenwaldt.)

of normal salt solution or Ringer's solution on an ordinary glass slide. The drop of secretion may be obtained with a platinum loop from the vault of the vagina after exposure with a speculum. A more simple method is to make a vaginal examination and on withdrawal, a moderate amount of secretion will be found adherent to the gloved fingers. One or more drops may easily be placed on cover slips or slides. If the latter method is used and the glove is dry when drawn on, the dusting powder should be washed off with soap and water before making the vaginal examination. No antiseptic or lubricant should be used on the glove. For studying the organism, fields should be selected where there is relatively little discharge, namely, at the periphery of the drop of secretion. The drop usually consists of a large number of leucocytes and bacteria, many epithelial cells and

many trichomonas. With the ordinary high power lenses the parasites may be readily seen because of their motility.

The Trichomonas vaginalis varies considerably in size. Usually, however, it is larger than a polymorphonuclear leucocyte, but smaller than an epithelial cell. The measurements given by various individuals are as follows: Rodenwaldt, length 12 to 30 μ, width 8 to 18 μ; V. Prowazek, length 12 to 30 μ, width 10 to 15 μ; Hegner, length 7 to 21 μ, width 6 to 18 μ; Bensen, length 16 to 26 μ, width 6 to 18 μ; and Reuling, length 10 to 30 μ, width 10 to 15 μ. The organism varies in shape also. Usually, however, it is spindle shaped or pyriform. (Figs. 1, 2, 3, and 4. The front end is rounded and from it protrude

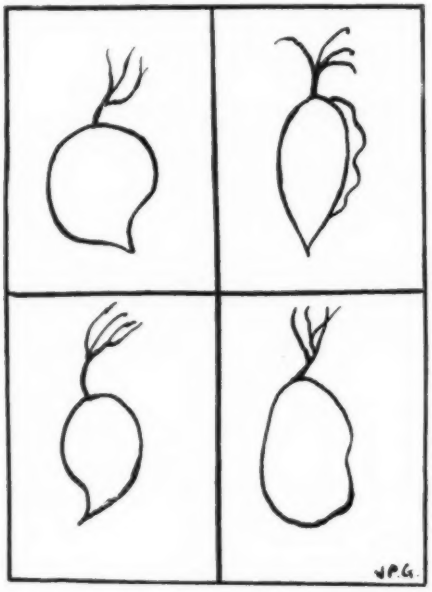

Fig. 2.—Simple outline drawings of trichomonas. All the organisms have four flagella, and one shows the undulating membrane.

four flagella which arise from a common stem. The older writers believed there were only 3 flagella, but Reuling in 1921 definitely proved there were four. The flagella arise in pairs, are approximately of the same length, and are more than half as long as the body of the organism. The point of origin of the flagella is a group of large, dark blepharoplastic granules and at this site the capsule is retracted. Starting from another dark granule near the base of the flagella, an undulating membrane runs somewhat spirally along the entire body to the posterior end which is usually pointed. Between the origin of the flagella and the undulating membrane is a light tubular organ. The protoplasm of the organism is not homogeneous but consists of

myriads of fine granules. Throughout the cytoplasm are small vacuole-like areas which are irregular in number and shape and show a distinct fat reaction with Sudan III. The nucleus of the trichomonas is usually eccentrically situated near the base of the flagella and is oval or pyriform in shape. In the fresh hanging drop preparation the parasite is in constant motion. The movement of the flagella is somewhat similar to that of a fishing line when cast. The flagella first strike sideways, then they undergo a circular movement toward the middle and finally the free ends turn inward. By means of this motion the flagella force bacteria, cellular detritus, and fat droplets toward the tubular organ where they disappear, hence this is most likely the

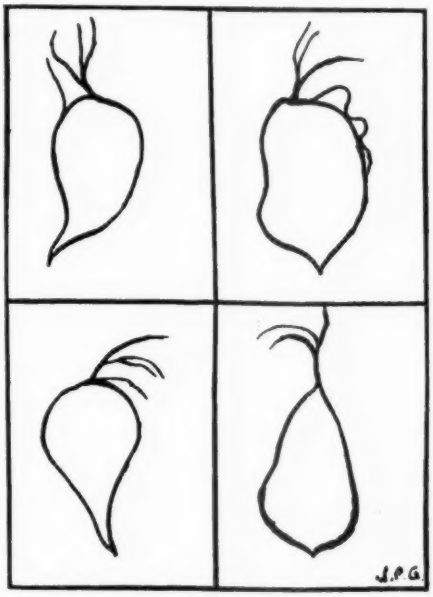

Fig. 3.—Two organisms in this group have only three flagella and one shows an undulating membrane.

mouth. The locomotion of the organism is independent of the flagella but is dependent upon the undulating membrane which is always found on the side where it can move freely. Occasionally, however, locomotion takes place by extrusion of pseudopodia and ameboid activity. Pseudopods are also extruded for purposes of phagocytosis of leucocytes and bacteria. Notwithstanding what some authors say, detection of the trichomonas in stained smears is easy to one who is familiar with these flagellates. The Gram stain is the one of choice and the best results are obtained if the contrast solution is permitted to remain on the slide a little longer than is customary. The organism may also be stained with Heidenhahn's iron hematoxylin after moist fixation with bichloride alcohol (Schmid and Kamniker) or fixation

with Schaudinn solution (Hegner). For making slides, the discharge which is high up in the vault and close to the vaginal wall should be used and not the discharge which is on the surface.

Cultures of Trichomonas vaginalis are hard to make but good media are blood serum diluted with sodium chloride, Locke's or Ringer's solution (Lynch), half ascitic fluid and half Ringer's solution (Ohira and Noguchi), sodium-chloride-serum water (Hoague) and ten parts of nephritic urine to one part of blood serum (Schmid and Kamniker).

The Trichomonas vaginalis nearly always lives in symbiosis with other organisms, usually bacteria and most often the latter are gram-negative cocci which are smaller than gonococci. In most cases the

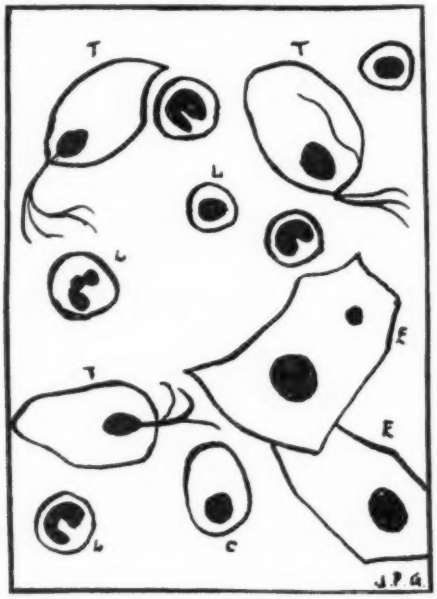

Fig. 4.—Gram stain. *T*, trichomonas; *C*, cyst form of trichomonas; *E*, epithelial cell; *L*, leucocyte.

bacterium found is the micrococcus aerogenes alcaligenes. The gas bubbles which are present in the vaginal discharge of many cases are produced by these micrococci according to Schröder, Löser, Schmid and Kamniker. The association of the gonococcus and trichomonas is very rare.

Without any special precautions the trichomonas can be kept alive at room temperature for three or four hours. Attempts made by Hoague to inoculate cats, kittens, and rabbits with trichomonas were unsuccessful. Likewise Blochmann failed to inoculate rabbits and Dock could not transplant the organism in guinea pigs, rabbits, and dogs. However, Kessel recently experimentally established Trichomonas hominis from man in ten of fourteen kittens.

CLINICAL COURSE

The clinical picture produced by the Trichomonas vaginalis when it is pathogenic is rather uniform and striking. The patients complain of a profuse discharge which in about half the cases is associated with a burning or itching sensation in the vagina and on the vulva. In some cases the irritation is so severe that sleep is disturbed. The patients often scratch the external genitalia and an inflammatory reaction similar to intertrigo may result. Often the discharge has a very disagreeable and penetrating odor.

On external examination small condylomas either flat or pointed, may occasionally be seen but the introitus is usually reddened. The entire vaginal mucosa all the way up to the vault is found to be reddened and sometimes it is fiery red. In the introitus the redness is usually diffuse but in the vagina it may be diffuse or patchy. Often the vaginal mucosa has a deep orange color, and usually it presents the appearance of an inflammatory condition. For this reason the clinical picture is called Trichomonas vaginalis vaginitis. The region of the external os is also usually red and it occasionally bleeds readily even though there is no erosion. No inflammatory condition, however, is found above the external os. The vagina contains a very large amount of greenish, yellow, foamy pus which looks like gonorrheal pus; but sometimes the discharge is thin and watery. Most of it is found in the vaginal vault and it may have an acid, alkaline or amphoteric reaction. Some patients are nervous due to the constant irritation, sleeplessness and fear of having contracted a venereal disease. Many go from doctor to doctor and while they secure temporary relief, they are not cured. Quite a few women are unclean in their personal habits but by no means all.

TREATMENT

Hoehne advocated the following treatment which others have used with slight modifications. The vagina is thoroughly washed with a 1 per cent solution of bichloride of mercury and dried and the vaginal wall is covered with glycerin which contains either borax or soda. The vestibule and labial folds are likewise treated. This treatment is repeated daily for four days or four times in one week. However, to maintain the cure, the glycerin mixture must be used daily for a while, then every second day and so on, gradually increasing the intervals between treatments. Hoehne prescribed capsules which contained 10 per cent borax or soda in glycerin so the patients could treat themselves after the first course of four treatments. Schmid and Kamniker treated 81 patients in this manner and obtained cures in 80.3 per cent. Recurrences were reported in 21 per cent. In 1919

DeLee advocated putting the patient to bed for two days during which time she received the following treatment. On the first day the vagina and vulva are scrubbed vigorously with green soap and water, using a rough cloth. The soap is rinsed out with sterile, distilled water. Then a 1-1500 bichloride of mercury douche is given and this is also washed out with sterile, distilled water. The next morning the vagina is again scrubbed with green soap and water and it is packed with cotton soaked with 4 parts of glycerin and 1 part of sodium bicarbonate. The following morning the tampon is removed and a sterile water douche is given. Baking soda douches are then prescribed twice daily.

The treatment I used in the present series of cases is as follows: The vagina is very thoroughly scrubbed with gauze saturated with tincture of green soap. All the vaginal folds are smoothed out and every part of the mucosa is scrubbed. The vulva is likewise scrubbed and the region around the anus. This scrubbing is one of the most important steps in the treatment and it is usually persisted in until very slight bleeding is noted in the vaginal mucosa. The soap is washed out with water and then the vagina is thoroughly dried. A tampon which is saturated with a methylene blue solution is inserted through a speculum high up into the vaginal vault. A second dry tampon is inserted to prevent the escape of the solution onto the patient's clothes. The vulva is lightly painted with the methylene blue solution. The patient is instructed to remove the tampons in the evening before going to bed. The string of the second tampon has a knot tied in it so the patient may know that this tampon is to be pulled out first. Because the methylene blue solution stains everything and can hardly be removed, the patient is advised to undress completely before removing the tampons and this is preferably done while in a bathtub. After removal of the tampons a douche containing 0.5 per cent lactic acid is taken. The treatment outlined is repeated every second day for three or more times. The patient takes a lactic acid douche on the mornings between treatments but not on the mornings she is to receive a treatment. No douche is taken on the morning of a treatment because we wish to see how much discharge there is and we also make hanging drop examinations. If the hanging drop on two successive visits fails to show trichomonas no further methylene blue treatments are given. However, the patient is advised to take a lactic acid douche daily for about two weeks. The purpose of the lactic acid douche is to attempt the reestablishment of a normal bacterial flora in the vagina. A matter of importance but unpleasant to discuss is the cleansing of the anus after a bowel movement. Most women use an upward sweep toward the vagina but this may produce reinfection if the causative organisms come from

the rectum. The patients are instructed to use a sweeping motion directed away from the vagina and toward the sacrum.

The formula for the methylene blue solution we use is as follows:

Stock Solution	
Methylene blue crystals	1 ounce
Distilled water	10 ounces
Solution Ready for Use	
Stock solution	25 c.c.
Glycerine	64 c.c.
Distilled water q. s. ad	1000 c.c.

RESULTS IN 56 CASES

I have treated 56 private patients by the green soap-methylene blue-glycerine-lactic acid method outlined above. All of these sought advice and treatment for a persistent, irritating, or obnoxious vaginal discharge.

The age of the patients is given in Table I. The youngest was twenty and the oldest fifty-one years of age.

TABLE I. AGE

20 to 25 years	11
26 to 30 years	22
31 to 35 years	12
36 to 40 years	6
41 to 45 years	3
46 to 50 years	1
51 years	1
	56

The parity is listed in Table II and it will be noted that 32.7 per cent of the patients had never been pregnant and that 21.4 per cent had had miscarriages before being treated for their vaginal discharge.

TABLE II. PARITY

Nullipara	19
Primipara	22
Secundipara	11
Tertipara	3
Sextipara	1
	56

The number of treatments is shown in Table III. The patient who received one treatment did not return for more. Most of the patients received two, three, or four treatments and I believe now that all patients should receive at least three. The recurrences were more easily cured because in 5 cases out of 14 only 1, and in 4 cases only 2 treatments sufficed. Two patients received the therapy suggested by Dr. DeLee after having been treated by the aforementioned scheme.

One of these patients was cured but one is listed among the failures. Some recurrences are perhaps due to persistence of the cyst forms of the trichomonas as described by Bensen.

TABLE III. NUMBER OF TREATMENTS

	FIRST COURSE	RECURRENCES
1	1	5
2	11	4
3	26	4
4	12	
5	5	
6	1	1
	56	14

Table IV shows the time of recurrence in the ten patients who had a total of 14 recurrences. Three patients had a second and one patient a third recurrence. The time of recurrence varied from one to fifteen months.

TABLE IV. TIME OF RECURRENCE

	FIRST	SECOND	THIRD
1 month	1		
3 months	4	1	1
4 months	2	1	
5 months	1		
8 months	1		
11 months	0	1	
15 months	1		
	10	3	1

In Table V the results of the treatment are shown. Of the 48 patients followed up 38 (79.2 per cent) were cured after one series, and 5 (10.4 per cent) after repeated series of treatments. The total number of cures was therefore 43 (89.6 per cent). In the patients who were cured, it was noted that the amount of discharge, the number of pus cells and the number of trichomonas ran parallel. When the parasites were destroyed, the character of the discharge changed, the amount decreased to practically normal, the inflammatory changes in the vaginal wall disappeared and the subjective symptoms vanished. There were five failures (10.4 per cent) and all of these women are high-strung, sensitive individuals. Their constitutional make-up evidently plays a part in the persistence of the vaginal discharge, because in four of these cases the discharge is troublesome only when the women are mentally upset.

TABLE V. RESULTS

Number of patients followed up	48 out of 56 (85.7 per cent)
Number cured after one series of treatments	38 out of 48 (79.2 per cent)
Number cured after repeated series of treatments	5 out of 48 (10.4 per cent)
Total number of cures	43 out of 48 (89.6 per cent)
Number of failures	5 out of 48 (10.4 per cent)

Table VI shows the duration of cure which varies from two to forty-eight months. Some of the patients listed as cures for the first twelve months may have recurrences in the future.

TABLE VI. DURATION OF CURES

2 months	2
3 months	1
6 months	2
8 months	3
10 months	2
11 months	2
12 months	1
13 to 18 months	6
19 to 24 months	9
25 to 30 months	5
31 to 36 months	2
37 to 42 months	5
43 to 48 months	3
	43

Among the 56 patients in this series there were eight whom I treated during pregnancy. The treatments were not as vigorous as in the nonpregnant women but they probably helped to prevent morbidity during the puerperium. As mentioned before, Gragert, Liss, Schmid and Kamniker reported that most women who have a Trichomonas vaginalis discharge during pregnancy have fever during the puerperium. Seven of my patients went to term and delivered as follows: spontaneous 3, low forceps 3, and cesarean section 1. The puerperium in these seven women was entirely uneventful. The eighth patient had a spontaneous miscarriage which was not followed by any complications. In addition, two women who were cured five months and twenty months ago respectively, are now pregnant and thus far the discharge has not returned.

In 19 cases after the vaginal discharge had been freed of trichomonas, the cervix was treated with the electric cautery because of a pathologic condition. In two additional cases the cervix had been cauterized before the Trichomonas vaginal discharge appeared. In this series of 21 patients treated with the cautery, eight patients (33.3 per cent) are listed in the group of recurrences of the trichomonas discharge. Three of the five failures were in this group of patients.

On six patients after clearing up the vaginal discharge, I performed a Rubin tubal patency test without any complication. The tubes were found to be patent in four and closed in two cases. From one patient I removed a Bartholin gland cyst without any complications. In three patients, trichomonas were found in the urine but the patients had no urinary symptoms. Systematic examination of the urine would probably have yielded a larger number of such findings.

SUMMARY

This report deals with 56 patients who complained of a persistent, irritating, foul, vaginal discharge, the cause of which was the Trichomonas vaginalis. Among 48 patients followed up, 89.6 per cent were cured after one or more series of treatments. The duration of the cure varies from two to forty-eight months. Failures were encountered in 10.4 per cent. While the results are fairly good, other forms of treatment are being studied in an attempt to help those patients who do not yield to the green soap-methylene blue-glycerine-lactic acid treatment. The point to be especially emphasized is that when a patient complains of a persistent, itching or burning, vaginal discharge which is yellow-green and bubbly and the vaginal mucosa is reddened, the diagnosis of Trichomonas vaginalis vaginitis can be made with great probability. To make the diagnosis certain, the simplest procedure is to examine a drop of the fresh discharge either as a hanging drop or on a flat slide.

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(For discussion, see page 897.)

CHOREA GRAVIDARUM*

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SINCE prenatal care has become an important part of the service rendered to the patient, the various complications of the gravid state have received more serious consideration.

It is my purpose to consider chorea gravidarum (which in its major form is one of the rarer diseases associated with pregnancy) because of its serious possibilities, and because in a review of the literature covering a period of twenty-five years, I have found that conceptions concerning its etiology, histopathology and treatment have undergone considerable modifications.

Chorea is such a rare complication of pregnancy that few individual practitioners have had a large personal experience with it, and many of the articles reviewed in the literature are simple recitals of case reports. Williams, in the latest edition of his textbook on Obstetrics, states he has seen only one grave case and that the patient died in spite of a premature spontaneous delivery.

The disease was first described by Schenkius in 1594 and by Horstius in 1660. As early as the latter half of the seventeenth century different authors called attention to the gravity of chorea in pregnant women. In 1869 Barnes collected fifty-six cases with seventeen deaths and noted that it was one of the most dangerous complications of pregnancy. He observed that patients will recover whether labor is induced or not, and that other patients die in spite of the interruption of the pregnancy.

With regard to the etiology of the disease there is a preponderance of evidence to support the belief that it is of infectious origin; that the usual seat of infection is in the brain and heart, with a predilection in the brain for the basal ganglia and in the heart for the endocardium, and more particularly the mitral valves. In cases autopsied, lesions of the endocardium have been found and Raymond, in addition to these, also found pathologic changes in the corpus callosum and the cerebrum. Raymond's observations on the suprarenals and the corpus luteum were negative, thus eliminating the part that these ductless glands were thought to have played in this complication of pregnancy.

LaPage suggested that lesions be looked for in the corpus striatum and in the optic thalamus in which lesions had been found in chorea.

Creutzfeldt, in 1924, reported a case in which he found lesions in the cerebrum, following the course of the vessels, the most severe degenerative processes being located in the striate body.

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Genova (1921) reported two cases of chorea gravidarum; both patients had rheumatism before the chorea, and after a review of the history of the disease and the theories as to its etiology, Genova stated that the most reasonable hypothesis is a toxico infectious origin of the disease.

Some observers believed that chorea gravidarum was a toxemia of pregnancy due to the absence of the menses and to toxins of fetal origin. It was suggested that it was due to defective elimination by the organism of toxins both exogenous and endogenous having a selectivity toward the nervous system and the joints. Choreic symptoms frequently occur toward the third month of pregnancy, favoring the theory that it is a toxemia.

While the theory of toxemia still has its adherents, it is my belief that careful autopsy examination will reveal in every case the presence of an infectious process. It is interesting to note, in this relation, that with one exception in my survey of the literature, no autopsy findings were recorded which showed changes found in the other fatal toxemias of pregnancies, viz., degeneration in liver, kidneys, heart muscle, etc.

Many observers have noted a neuropathic constitutional tendency as a predisposing factor to chorea, while a lesser number believe that heredity plays an important part. Some observers, such as Whitmore, have gone so far as to state that it is a pure neurosis. Exciting causes are traumatism, fright, and emotional conditions associated with hysteria. Neurotic mental symptoms frequently precede the attacks.

Flamma in 1919 reported a case of supposed chorea in which he feigned an interruption of pregnancy and found it to be a pure neurosis. This patient had lived with a choreic patient. Flamma and others warn against the interruption of pregnancy without evidence of a positive diagnosis of chorea.

Infections of known streptococcal origin, such as scarlet fever, rheumatic fever, and endocarditis often precede chorea gravidarum.

Fraiport reports fifty autopsies in which valvular lesions were found in 66 per cent.

The condition is more common in young women and more common in primiparae. It is also more common in those who have had previous attacks of chorea. It may or may not recur in later pregnancies. Martin reported a group of cases in which chorea was absent in the first and present in later pregnancies and we have observed two cases of chorea occurring during the second pregnancy.

The study of the choreic forms of lethargic encephalitis has added to the knowledge of the pathology of chorea. Marie and Tretiakoff examined the nervous system of a case of typical Saint Vitus dance in a child ten years old and found lesions in the neostriatum and central cortex similar to those of epidemic encephalitis. Evidence has accumulated to make it apparent that the pathologic basis of Syden-

ham's chorea may be a diffuse encephalitic process involving the cortex, pia, arachnoid, and the corpus striatum. The caudate and putamen are also affected.

The macroscopic changes are very slight and usually absent. This may account for negative autopsy reports in the literature and suggests the importance of microscopic examination of the brain in all fatal cases of chorea gravidarum.

Greenfield and Wolfson, reporting on the postmortem findings in a case of Sydenham's chorea, described in addition to a vegetative endocarditis, small, round cell, perivascular infiltration in the basal ganglia, and internal capsule similar to those of lethargic encephalitis except the white matter was more involved. They also found thrombi in the cortical vessels but they found no evidence of cerebral embolism, such as has been reported by others.

Lewy studied a series of cases in which the disease process was not confined to the corpus striatum; in addition to foci of cell degeneration in the neostriatum there was evidence of cell changes and fatty infiltration in the cortex. The foci in the striatum showed acute degeneration of the small ganglion cells, with ameboid transformation of the striae adjacent to the glial cells. These neuroglia changes were present in the acute forms.

The old theory that cerebral emboli were responsible for the disease is not supported by pathologic findings.

Marie, Bouttier and Trétiakoff recorded an observation of a very severe acute chorea in a twenty-one-year-old pregnant woman. The first indication of illness followed upon a short neurasthenic prodrome during the beginning of pregnancy. At the end of two months death followed. In the uterus was found an 8-mm. embryo. On histopathologic investigation they found in the cortex of the hemispheres and striatum nodules varying in size from very minute areas up to the size of a pin-head which consisted of perivascular glia proliferation with destruction of the adjacent nervous tissue.

Creutzfeldt, 1924, described a fatal case in which he made a histopathologic study, from which he concluded that the findings in the nervous system consisted in an inflammatory type of disease with hyaline degeneration which attacked both gray and white matter, the localization being dependent upon the course of the vessels. The more marked degenerative processes were found in the striate body where they involved particularly the smaller ganglion cells. He thought that the anatomical location of the lesions could be correlated with the location of the choreic movements. Lehoczky-Semmelweis similarly observed in a fatal case which began during pregnancy with fever and arthritis, that in addition to parenchymatous degeneration of heart, liver, and kidneys, there was edema of the meninges and hyperemic spots in the basal ganglia. Microscopic investigation revealed perivascular infiltration in the striatum, thalamus, and substantia nigra. The cellular elements of the infiltration consisted chiefly of lymphocytes, but a few plasma cells were present and a few pigment-containing macrophages were found in the substantia nigra. There was necrosis of the nerve cells in the putamen and globus pallidum accompanied by glia proliferation.

The chief symptoms of chorea, whether occurring in the gravid or nongravid state, are involuntary and irregular purposeless movements of any or all of the muscles of the body. In severe cases the whole

body may be involved. Oppenheim, however, refers to rare cases of chorea where the movement is limited solely to the muscles of speech, eyes, lips, tongue, pharynx, and larynx. The intensity of the contractions varies and it is reasonable to assume that the violent uterine contractions occurring during chorea may be a frequent cause of premature expulsion of the fetus. The muscles of the hands, fingers, face, and tongue are most often affected but the legs and trunk muscles may also be involved. The patient may throw herself out of bed, bite her tongue, abrade her skin, or otherwise injure herself, which injuries may result in infection. The patient may become absolutely incompetent mentally, and in one of our patients it was necessary to place her in a restraining sheet both before and after emptying the uterus. Oppenheim used the term "muscular insanity" to describe the involuntary, irregular, and purposeless movements. In many cases the choreic movements cease during sleep but in the severer forms the movements are continuous and greatly aggravate the exhaustion, which is one of the causes of a fatal termination in chorea.

The most superficial examination is usually sufficient to establish a diagnosis of chorea gravidarum. Probably the most difficult task is to distinguish it from hysteria which can usually be differentiated from true chorea by the presence of other stigmas of hysteria and by the rhythmical character of the hysterical movements which are usually absent when the patient thinks she is not being observed. Flamma warns against the interruption of pregnancy in neurotic cases simulating true chorea, and we strongly recommend consultation with a neurologist in all cases of chorea gravidarum.

DeLee states that the maternal mortality in chorea gravidarum is from 20 to 30 per cent while the fetal mortality is 50 per cent. Other authorities estimate maternal mortality to run from 10 to 75 per cent. Backaus says that chorea in general is less serious for a child, more serious for a man, still more serious for a woman, and most serious for a pregnant woman. The fetal prognosis depends on the time when the fetus is expelled, on the severity of the choreiform contractions, the amount of asphyxiation of the fetus from heart lesions and other conditions in the mother, and upon the degree of septicemia of the mother. Muhlbaum stated that the predominance of psychic over motor delirium indicates an unfavorable prognosis. Royston concluded that pregnancy in a choreic individual is not necessarily serious although it may assume this character, but that an acute chorea beginning during pregnancy is always a grave affection. I believe that the high mortality, both maternal and fetal, consequent in severe chorea gravidarum, is not generally recognized by most physicians.

Concerning the treatment of chorea gravidarum there are two extreme schools, one in which the most radical treatment is recommended and the other in which the most conservative methods are advised.

LaPage strongly recommended emptying the uterus promptly in severe cases because he feels that the mortality in delayed cases is extremely high. In this opinion many authorities concur. I believe that chorea gravidarum is always of infectious origin and if we are correct in this assumption we are correct in assuming that the value of any medical treatment, with the exception of rest and quiet, is doubtful. Fletcher Shaw, Wall and Andrews, Croft, and others in England have reported a large number of cases successfully treated without the induction of premature labor.

Bonhoeffer states that over half of the cases of chorea gravidarum are harmless and result favorably, and we believe that this is, generally speaking, true. Muhlbaum has observed that most of the milder cases are treated by the neurologist and are not seen by the obstetrician. He further observed that an attack of chorea occurring first during pregnancy, accompanied by marked motor disturbances, forms an indication for the interruption of pregnancy. Hellier strongly advised terminating pregnancy in severe cases and stated the following indications for evacuation of the uterus: When there are violent movements in spite of rest in bed and sedatives; when there is inability to sleep or eat enough, accompanied by loss of weight; when the mental conditions are confused and when there is tendency to delirium; when there is a rise in temperature, a dry tongue, and especially, and he accentuates the following point: when the pulse is persistently above one hundred and is becoming weaker and more rapid.

Bumm, Martin and Anton recommended vaginal cesarean section as a rapid means of emptying the uterus in these cases. DeLee suggested abdominal cesarean section when the choreic gravid patient is at or near full term, and Jakoby reported a case delivered by cesarean section in December, 1925. Various medical treatments have been used, such as salvarsan (Hartel and others), arsenic, aspirin (Wall and Andrews), blood serum from a healthy pregnant woman (Albrecht), endocrine therapy (Haneborg), chloral, bromides and other sedatives, but it is our personal opinion that with the exception of sedatives in the cases of recovery in which these medicaments were used, the patients recovered in spite of, and not because of the treatment.

We desire to most strongly recommend absolute rest and quiet in all cases of chorea gravidarum, however mild or severe.

The following cases represent two distinct types of the disease, one being a severe form in which conservative treatment failed and the uterus was emptied by abdominal cesarean section.

CASE 1.—Mrs. E. D., aged twenty-six, married, secundipara, was admitted to Blodgett Memorial Hospital on August 1, 1925, complaining of continuous twitching and jerkings of the arms and legs. She first noticed an occasional twitching in the right arm about three weeks previous to admission which became worse and spread to the right leg and to the right side of the face. Four days before admission she had almost continuous jerkings. Her past history was negative for chorea and rheumatism. The patient had a tonsillectomy and adenoidectomy at the age of fifteen on account of repeated throat infections. With her previous pregnancy she had twitching of the right arm on the day of delivery, but this lasted only one day. Family history was negative.

On examination the patient was found to be about eight months pregnant. She

was of a tall, slender build with typical adenoid facies and protruding upper teeth. There were marked purposeless movements of the right upper extremity with picking at the bed clothes, and there was an occasional jerking movement of the right leg and irregular twitching of the facial muscles on the same side. These movements persisted during sleep. The patient exhibited mental confusion, was disoriented at times, and talked incoherently. The heart tones were clear, and no foci of infection were found. Blood pressure 110/72. The urine was negative for albumin and casts, the white blood count 4,750, blood Wassermann and spinal fluid Wassermann were negative. N.P.N. was normal and blood culture was negative on three successive days.

On the second day the mental symptoms became worse and she developed numerous hallucinations, chiefly auditory and on the basis of these, persecutory delusions. The choreic movements became more marked until the nurses were unable to keep her in bed without the use of a restraining sheet.

Treatment consisted in eliminative measures plus large doses of chloral and bromides which were augmented by the use of morphine and scopolamine, but her condition grew progressively worse until she became almost unmanageable. Therefore, on August 4 she was delivered by classic cesarean section of a living male infant weighing 6 pounds and 15 ounces. The child did not nurse well and presented two definite developmental anomalies, a facial asymmetry and a marked microphthalmus.

For the first few days postoperative, movements were marked and a restraining sheet was necessary, but movements decreased and the mother made a slow but for the greater part uninterrupted recovery. On August 8, she exhibited only slight twitching of the right arm, although she remained mentally confused. Gradual improvement continued and on the fourteenth day she was able to write. The patient left the hospital in good condition on August 30 and a letter from her dated July, 1926, states that both she and the baby are now in excellent health.

CASE 2.—Mrs. G. B., aged twenty-seven, married, housewife, secundipara, reported to the clinic on March 14, 1927, complaining of twitching over the entire body and salivation. This trouble began about March 1, 1927, following a period of nervous strain.

The patient has always been of nervous temperament and given to fits of laughing and crying. She was treated for chorea about one year ago. Tonsillectomy was performed in December, 1926, following which she felt well until about two weeks ago when she began to have symptoms as described. She has one child four years old; had kidney trouble during the pregnancy and convulsions (eclampsia) but no choreic movements. Menses began at fifteen, regular, twenty-eight-day type, lasting four days. Last period December 12, 1926.

The patient's mother had a nervous breakdown and also had twitchings of hands during pregnancy.

Examination showed a slender woman of evidently unstable nervous type, heart tones clear, B.P. 110/65. There was a slight relaxation of the vaginal outlet, bilateral laceration of the cervix with erosion of the anterior lip and a small polyp. Uterus was enlarged to size of three months' pregnancy, in good position, and otherwise negative. There were frequent twitchings of the hands, facial muscles, arms, and shoulders, and occasionally other parts of the body. A diagnosis of chorea in pregnancy was made and neurologic treatment advised. She was treated with bromides and rest and gradually improved although she continued to be nervous. Progress was then normal until July seventh, when she began to show a slight rise in blood pressure. Two days later a trace of albumin appeared in the urine. In spite of restricted diet the pressure continued at a level of about

140/110 with albumin in the urine, and on July twenty-seventh, casts were found. This condition persisted in approximately the same degree throughout the month of August. Near the end of the month slight edema appeared. On September third the pressure had risen to 150/100, and on the seventh to 180/120 when she began to have severe headache. At this time she was placed in the hospital, a milk diet prescribed and bromides and chloral administered per rectum. The next morning she complained of spots before the eyes and nausea. Blood pressure 178/110; eye grounds negative; N.P.N. 31. Some twitching of arms and eyelids noted. During the night she complained of stiffness of the right side of the face, and the nurse noticed that she talked through the left side of the mouth. The next morning she exhibited a right facial paralysis of the peripheral type. Blood pressure still elevated.

Under gas anesthesia a Voorhees bag was inserted at 11:30 A.M. The patient expelled the bag and gave birth to a 4 pound 10 ounce living male infant six hours later. Blood pressure 150/105 following delivery. Two days later the effects of the facial paralysis were marked. There were casts in the urine. The pressure returned to normal in the course of one week, but casts were still present and the condition of the facial muscles was unchanged. Then she began to have pain in the right side of the face and following this the paralysis gradually cleared. The infant gained rapidly and was in good condition on the date of discharge. There has been no recurrence of the choreic movements to date.

In each of the above cases several consultations were held with Dr. Frederick P. Currier, a neurologist, and there is no doubt as to the correctness of the diagnosis.

CONCLUSIONS

1. It is my opinion after reviewing the literature that all cases of chorea gravidarum are on an infectious basis and that accompanying lesions present in the endocardium and joints are of the same origin.

2. The pathologic changes consist of an inflammatory process located in the cerebrum, the most marked changes being in the basal ganglia.

3. Conservative treatment is sufficient for the mild and moderately severe cases, but the interruption of pregnancy must be resorted to in the extremely severe forms. Cesarean section may be performed when the child is at or near full term.

4. The dangerous possibilities of chorea gravidarum, both fetal and maternal, should be realized by all practitioners who do obstetric work.

5. Proper prenatal service with special reference to the removal of all foci of infection wherever practicable and with particular attention to the management of the neurotic patient from the standpoint of rest, both mental and physical, should reduce the incidence and severity of chorea gravidarum.

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(For discussion, see page 898.)

BACILLUS PYOCYANEUS BACTEREMIA OF PLACENTAL ORIGIN

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(From the Gynecological Service of Mount Sinai Hospital, New York City)

ALTHOUGH the pyocyaneus bacillus has been found in pure culture in all parts of the body, in localized lesions and in general systemic infections, it is only infrequently isolated in pure culture from the blood during life.

Numerous reports have been published in the literature describing cases of supposed generalized pyocyaneus infections, but a goodly percentage of these cannot be considered authentic. The Bacillus pyocyaneus, like the colon bacillus, is actively motile and is a frequent antemortem and postmortem invader of the body; and a large group of cases which have been regarded, heretofore, as general blood stream infections due to the bacillus of green pus, fall into the category of those cases in which the organisms were isolated from the blood only immediately before death or from the organs at the autopsy table and, therefore, cannot be classed as genuine pyocyaneus septicemias. The only so-called generalized pyocyaneus infections which can be accepted as authentic are those in which the bacilli are found in the blood during life or when they are found in numbers in the organs postmortem and seem to stand in causative relation to the changes in these organs. True pyocyaneus sepsis is uncommon.

According to Peet,[1] the first bona fide instance of pyocyaneus septicemia diagnosed by blood culture during life was that of a three months old child, reported by Finkelstein[2] in 1896. A positive blood culture was obtained two days before death. Brill and Libman,[3] in 1899, reported the second case in the literature in which the B. pyocyaneus was found in the blood during life in such a way as to exclude all doubts. This case was the first on record in which such a finding had been made in an adult. A positive blood culture was demonstrated two days before the patient's death.

A number of investigators, among them Wassermann,[4] Kolle-Hetsch,[5] Fraenkel,[6] and others believed that pyocyaneus septicemias were brought about, in most instances, after some other organism had produced a lowered tissue resistance. Waite[7] maintained that, not infrequently, the bacillus pyocyaneus was the primary and sole cause of the infection. Freeman,[8] in a very adequate review of systemic pyocyaneus infections, stated that the disease occurred in two forms, the acute and the chronic, and that it was a serious malady, often resulting fatally, although recovery occasionally took place. Klieneberger[9] pointed out, on the other hand, that the pyocyaneus bacillus may be found in the blood in transient septic manifestations, that pyocyaneus bacteremias were not as rare as generally considered, and that the long accepted opinion that a pyocyaneus blood stream infection meant a hopeless prognosis or a protracted and severe illness, had to be revised.

The portals of entry of the B. pyocyaneus are usually the skin, the external mucous membranes, the linings of the respiratory system and the intestinal canal, infrequently the genitourinary tract, and very rarely the gravid or puerperal uterus. After a very extensive search through the literature, the number of cases found of puerperal sepsis due to the Bacillus pyocyaneus were very few.

In 1889, Charrin[10] published an admirable treatise, *La Maladie Pyocyanique*, and therein suggested for the first time that the uterine mucosa may be a portal of entry for the Bacillus pyocyaneus and described a case of puerperal fever, in which this bacillus was associated with a few streptococci.

Perkins,[11] in an investigation of nine cases of pyocyaneus infection, reported two in which he attributed the focus of infection to the uterine mucosa. In the first instance the patient ran a course simulating tuberculous meningitis for six weeks following an abortion. The patient died eventually and cultures obtained from the uterus and cerebrospinal exudate at autopsy, nineteen hours after death, revealed the Bacillus pyocyaneus and other organisms. Culture of the heart's blood was negative. The second patient died of puerperal sepsis six weeks postpartum. Cultures from the uterus and lungs after death grew the pyocyaneus bacillus. The heart's blood was sterile. Whether Perkins' cases can be considered unequivocally as puerperal pyocyaneus septicemias is problematic inasmuch as the cultures were taken after death and, therefore, are of questionable value.

Rolly's[12] report, on the other hand, is infinitely more convincing. He described a case of general septicemia in a woman, who, simultaneously with the onset of profuse vaginal bleeding, showed signs of sepsis and meningitis. On the fourth day of her illness pyocyaneus was obtained in pure culture from the blood, and again on the eighth and tenth days of her disease in increasing numbers. She died on the eleventh day and the same organism that was found in the blood stream was cultured from the heart's blood, kidneys, spleen, intestines, and other organs. The autopsy revealed that the patient had been gravid. It was believed that the vaginal bleeding was due to the interruption of the pregnancy, that the gravid uterus was the source of the infection in the absence of any other portal of entry, and that the case was one of pyocyaneus puerperal sepsis.

There has not been found recorded, heretofore, a single instance of a transient bacteremia due to the Bacillus pyocyaneus in which the gravid or puerperal uterus was the origin of the infection. The following two cases were suspicious of a postpartum pyocyaneus bacillemia, but actual proof was lacking.

The first, mentioned by Walthard,[13] concerns a thirty-five-year-old multipara, who, on the third day postpartum, developed a chill and a substantial rise in temperature. Culture of the lochia revealed the Bacillus pyocyaneus and other organisms. No mention is made of blood cultures ever having been taken. After appropriate treatment the temperature dropped to normal and the patient recovered.

Delmotte's[14] case is quite similar. He reported the findings in a primipara, aged eighteen, who was delivered spontaneously and there were no injuries. Two days later, the patient developed considerable fever. The Bacillus pyocyaneus and a staphylococcus were isolated from the lochia. Blood cultures were negative. The patient recov-

ered. It is not unreasonable to assume that a transient pyocyaneus bacteremia may have been present at some time or other in each of these cases. That blood cultures were not obtained at just the proper moments to prove that point is unfortunate.

The following case from the Gynecological Service of Mount Sinai Hospital is probably the first to be reported of a pyocyaneus bacteremia of placental origin:

Mrs. B. A., aged thirty-four, a multipara, was admitted to the hospital November 13, 1927. She complained of vaginal spotting of two weeks' duration and cramp-like abdominal pains for three days. The family history was inconsequential. The personal history was unimportant except for erysipelas ten years ago. The menses began at fourteen and were always regular. She had been married twelve years and had been gravid four times. She had had two uninduced abortions, each taking place in the third month of pregnancy. Her youngest child was eight years of age.

The last menstrual period occurred August 4, 1927. About November first, the patient began to spot per vaginam and several days later passed numerous blood clots. Ten days after the onset, she experienced rather severe abdominal cramps. The family doctor made a pelvic examination under aseptic precautions on November 13 and advised hospitalization. The patient denied strongly that any attempt had been made to interrupt the pregnancy. Her story seemed quite straightforward.

Physical Examination.—Temperature 99.6°, pulse 94. The patient was a plethoric, rather obese, and well-developed German woman. She did not look ill. No marked abnormalities were noted in the general examination. Blood pressure was 122/50.

Pelvic Examination.—Moderate amount of foul vaginal bleeding. Relaxed introitus. Small cystocele and rectocele. The cervix was violaceous, soft and closed. The fundus uteri was enlarged to the size of a three months' gravidity, forward, freely movable and irregularly contracted. The adnexa were negative. The parametrial regions were clear.

Laboratory Examinations.—Urinalysis showed a trace of albumin and numerous clumped white blood cells. Hemoglobin, 70 per cent (Sahli). Sedimentation time, thirty-one minutes. Blood Wassermann was negative.

Clinical Course.—Twelve hours after admission, the temperature rose abruptly to 105°, followed by a severe chill. Blood culture, at this time, was positive for a gram-negative bacillus in all of the following media: (1) tomato extract of liquid peptone and glucose; (2) 2 per cent glucose bouillon; (3) plain bouillon; (4) plain agar; (5) 2 per cent glucose-agar with 33 per cent ascitic fluid; (6) liver hormone-agar with 33 per cent ascitic fluid. The organism was identified as Bacillus pyocyaneus, 20 colonies per cubic centimeter of blood. Anaerobic culture (Noguchi-Rosenau cooked liver media) was negative.

The patient received 1¼ c.c. of pituitrin intramuscularly in divided doses. The fetus was expelled spontaneously about four hours after the medication. The placenta did not come away and it could not be expressed. Immediately after the expulsion of the fetus the temperature dropped acutely to normal and did not rise above 100° during the patient's remainder in the hospital.

In spite of large amounts of pituitrin and quinine, the placenta remained in the uterus. Four days later, during which time the temperature had been normal, it was decided to remove the placenta instrumentally. Without anesthesia the external os was exposed after having painted the vagina with a weak iodine solution. The cervix was neither grasped with a vulsellum forceps nor was its canal dilated.

An ovarian clamp was inserted gently into the uterine cavity and the foul-smelling contents were evacuated with ease. The wall of the uterus was not curetted. The material removed was cultured immediately. The Bacillus pyocyaneus and the colon bacillus were recovered. Miscoscopic examination of the uterine contents showed infected placental tissue. After an uneventful recovery, the patient was sent home November 29, 1927, the sixteenth hospital day.

There is no doubt that this is an authentic case of a transient Bacillus pyocyaneus bacteremia of placental origin. The evidence is fairly conclusive. The presence of the same organism both in the blood stream and in the placental tissue is more than merely coincidental.

SUMMARY

1. Bacillus pyocyaneus septicemias and bacteremias are uncommon.
2. Puerperal sepsis due to the pyocyaneus bacillus is extremely rare.
3. The case herein described is probably the first to be reported of a transient Bacillus pyocyaneus bacteremia of placental origin.

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BELLEVUE HOSPITAL.

A SELF-RETAINING CANNULA FOR INJECTION OF LIQUIDS OR GAS IN TUBAL INSUFFLATION*

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WHEN the use of iodized oils was introduced for roentgenographic study of the uterus and tubes, there came with it the need of an instilling cannula possessed of the following features:

1. It should have a metal shoulder firmly attached to the tip in order to prevent back leakage; the rubber urethral tips formerly used usually slide on the metal shaft when they become oily.

2. It should be self-retaining in the cervix as this eliminates further the risk of leakage; it also permits the patient to be moved for roent-

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genographic study or for operation (in cases in which the surgeon wishes to observe the fluid injected while performing laparotomy) without the disadvantage of requiring an attendant to hold the cannula in position. To retain the oil in the fundus while roentgenographic plates are made the cannula is equipped with a pet-cock. A Luer syringe connection eliminates the use of all rubber tubing for the oil injections, and if used with a gas medium facilitates a snug connection (Fig. 1).

With the patient preferably in a Sims or knee-chest position, the technic consists of grasping the cervix either laterally or anteroposteriorly as desired with two 5.75-inch tenaculum forceps. The canal is then prepared by cleaning with gauze and painting with mercurochrome or iodine. The cannula is now gently inserted to the metal

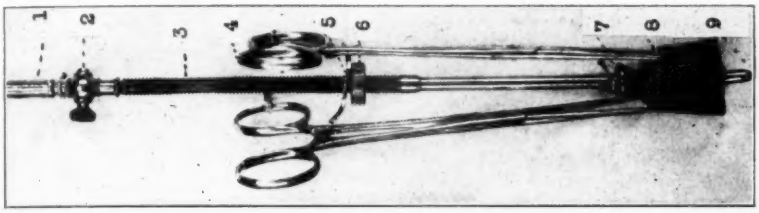

Fig. 1.—1, Luer syringe connection; 2, pet-cock, to retain iodized oil; 3, threaded portion of cannula; 4, two five and three-fourths inch tenaculum forceps; 5, sliding-collar with projection for forceps handles; 6, milled screw to regulate and maintain tension; 7, metal plug for cervical canal to prevent back leakage; 8, rubber cork, represents cervix; 9, perforated cannula tip.

shoulder. (These shoulders are made in two sizes but the large size may be used for all cervixes.) The forceps lock bars are then slipped over the projections on the sliding collar and the milled thumb-screw adjusted to produce a tight connection at the external os.

The instrument is not bulky and as the tenaculum forceps are separate, they can be used to steady the cervix while the cannula is being inserted.

My colleagues and I have used this cannula for more than a year and have found it to be entirely satisfactory. I am indebted to Mr. J. S. Hipple, of the University of Wisconsin, for his skill in the construction of the present instrument.

Society Transactions

THE CHICAGO GYNECOLOGICAL SOCIETY

MEETING OF JANUARY 20, 1928

DR. J. P. GREENHILL described a case of **Hematometra Following Labor.**

Mrs. E. L., a negress, thirty-five years old, married fifteen years, was admitted to Cook County Hospital January 19, 1928, complaining of severe pain in the lower abdomen, nausea and vomiting and a chilly sensation, for four months. Her first labor was terminated at term by craniotomy on a dead baby at Cook County Hospital, June, 1927. The patient developed a thrombophlebitis in the left leg and remained in the hospital for three weeks. The patient felt well until three months later when irregular attacks of pain in the abdomen began. On admission, examination showed an extensive amount of scar tissue which covered the lower abdomen and vulva, resulting from a severe burn in childhood. An indefinite mass above the pubis was difficult to outline because of the scar. The vaginal wall was smooth and the external os was flush with the vaginal mucosa. The cervix was entirely above the vaginal vault. The corpus was very soft, cystic, round, movable, and approximately the size of a three months' pregnancy. The lower part of this cystic uterus bulged into the vagina and rectum. The adnexa were negative. These findings, coupled with the fact that the patient had not menstruated at all during the seven months following delivery, made Dr. Greenhill venture a diagnosis of hematometra, but he considered a degenerated pregnancy as a second possibility. When he examined the cervical orifice with the speculum, the diagnosis of hematometra was confirmed, because across the small external os was a thin film which appeared blue in color. This film was incised and about 5 ounces of dark, tarry blood was permitted to escape slowly. The external os was dilated and when a finger was inserted into the uterus it was found that the lower half, the cervix and isthmus, were considerably dilated, whereas the corpus had contracted. (The patient made an uneventful recovery.)

DR. FREDERICK H. FALLS read a paper on the **Diagnosis of Fetal Deformities in Utero.** (For original article see page 801.)

DISCUSSION

DR. W. A. N. DORLAND said that there is probably no danger in x-rays used for diagnostic purposes and exposure of five to seven seconds is not likely to damage fetal tissue. If any damage were to result it would not be in the formation of monstrosities, these x-rays being taken from the third to the fourth month, at which time the embryo had attained its form. If any damage occurs, it would be in retardation of development of the fetus, either in the muscular or mental development. The cases that have been reported of such retardation in experimental work have probably resulted from too prolonged use of the rays, much longer than would be used for diagnostic purposes.

The recognition of monsters by x-ray prior to birth necessarily will be a slow process as the cases are comparatively infrequent.

DR. D. A. HORNER called Dr. Fall's attention to his inaugural thesis nine years ago in which he demonstrated three monstrosities by means of the x-ray, one of them an anencephalic monster and one a hydrocephalic monster. Dr. Horner doubted whether a definite syndrome can be developed clinically, because monstrosities will surprise the obstetrician by their presence regardless of any physical examination or x-ray picture that may be made. With visual inspection, palpation, percussion, and vaginal examination, one often comes to the conclusion that he is dealing with a monstrosity and at the time of labor finds some sort of malpresentation like a face presentation.

He thought Dr. Falls was right in warning against doing a cesarean section without an x-ray picture being made. He had done that and had been surprised after making a diagnosis and having an x-ray picture of a normal baby to find a monstrosity.

DR. W. H. RUBOVITS said there was a class of cases of abnormalities of the fetus which he considered worthy of attention. Six months ago he delivered a baby by cesarean section with edema of the skin which died on the third day. Clinically, nephritis was demonstrated. In relating the experience a colleague told him that he had a similar case in which an x-ray was taken before delivery. The position of the hands and legs indicated clearly that the fetus was suffering from a tremendous degree of edema of the skin, which was proved on delivery.

DR. J. P. GREENHILL said that five years ago he wrote a paper on the association of fetal monstrosities and placenta previa and since then he has been on the lookout for such cases. From his observations he felt that there is more than a casual relationship between the two conditions. Fairly presumptive evidence of this is the fact that at the Chicago Lying-In Hospital, with about 3,000 deliveries annually, almost half the fetal monsters were associated with placenta previa, during the last nine years.

He was in full accord with what Dr. Falls said about taking x-ray pictures in any case in which the fetal head is not definitely palpable. This is especially to be emphasized in placenta previa where monsters are not thought of.

Many obstetricians urge cesarean section because of the greater safety to the baby. It is very unpleasant to tell the parents this and then deliver a monster. Dr. Greenhill then showed a number of x-ray plates of various types of monsters in utero. Dr. Falls said that in 1925 Daub reported the first case of hydrocephalus detected by the x-ray, but Dr. Greenhill said that in 1923 in a paper on "X-ray in Obstetrics" he published an x-ray picture showing a hydrocephalus in utero.

DR. FALLS, in closing, said that if he is not sure he can palpate the fetal head externally he makes a vaginal examination. If, on palpation, there are abnormal fetal movements, or if the heart tones go down to an unwarranted degree, sixty, seventy or eighty, without evidence that the head is being unduly compressed by the pelvic bones, he takes an x-ray picture. He has never had a case in which he suspected the presence of anencephalic monster from these points which was not confirmed by the x-ray examination. Spina bifida will not give this syndrome. There is no change in the heart tones. There is no difficulty in palpating the head and unless for some other reason one makes an x-ray examination the deformity will not be found before delivery.

Dr. Rubovits' presentation of the fetus in peculiar position reminded him of a case in which he made a similar diagnosis in 1917 and in which there was no abnormality of the fetus such as a tumor of the neck or edema of the skin but in which there was complete opisthotonos. He made the diagnosis because he could not keep the head over the inlet. The baby was in the transverse position. He

reported the case in *Surgery, Gynecology and Obstetrics.* As far as he could find there were no other cases of that kind reported, although Williams said there were some drawings of this kind in the old German textbooks and Dr. DeLee said he had seen a case but had not reported it.

As far as placenta previa and monstrosities are concerned, Dr. Falls said if he found a central placenta previa, even if he knew it was associated with a monstrosity, he would treat the central placenta previa and disregard the deformity. In central placenta previa he considers cesarean section the safest procedure. In other types of placenta previa he would be inclined to avoid doing a cesarean section in the case of a monstrosity because the value of saving such a baby is nil.

There is danger in a misinterpretation of x-ray pictures. Recently he had occasion to x-ray a patient and the report came back from the laboratory, "fetal death because of overlapping of the skull bones." He was able to hear the heart tones and diagnosed and delivered a live baby, notwithstanding the fact that he felt the interpretation of the x-ray picture was right. Therefore, until further observations are made, he should hesitate to make a diagnosis of fetal death merely from apparent overlapping of the skull bones.

THE CHICAGO GYNECOLOGICAL SOCIETY

MEETING OF FEBRUARY 18, 1928

DR. O. S. PAVLIK read a paper entitled **Preservation of Ovary by Means of Intrauterine Transplantation in Radical Operations for Adnexal Disease.** (For original article see page 867.)

DISCUSSION

DR. W. McI. THOMPSON said that in his experience the vascular pedicle is the essential requisite in transplanting an ovary. Only where the ovary was transplanted with a vascular pedicle has he had any success in retaining its function.

DR. JOSEPH L. BAER believed that the transplantation of the detached ovarian tissue, however it may be preserved or wherever it may be placed, is of so temporary a value as to be comparatively futile and carries with it an element of risk, for, if the ovary is in a subject who has acute or subacute adnexal disease there is likelihood of infection secondary to the transplantation. If then, the better scheme is to preserve the ovary with its vascular supply when feasible, why would it not be preferable to preserve the ovary in situ in proper relation to the broad ligament rather than to insert it into the uterine cavity. If the ovary can be preserved at all, it would be better to trim off the diseased tube and leave the ovary free on its pedicle and in its comparatively normal relationship to the broad ligament. That has been his practice over a considerable period of time. In his experience such an ovary may undergo cystic degeneration during the first half year following operation. If that patient is seen by some other operator during that period he may say she has an ovarian cyst that should have been removed by the previous operator, whereas if the patient is left unoperated for a year the cyst subsides and the patient has to all intents and purposes a normal ovary. For this reason he is doubtful of the value of dislocating the ovary which retains its vascular supply.

DR. CARL H. DAVIS said he wished to second the remarks of Dr. Baer but to differ from him in one particular. Sometimes it is not possible to leave ovarian

tissue in the abdomen and yet from a purely psychologic point of view it is worth while to transplant a piece of ovary into the rectus muscle and within three months there will be evidence of ovarian function. Periodic enlargement of this ovarian tissue can be followed for several years. The very fact that the woman knows she has ovarian tissue is going to be of value to her mentally even though it gives nothing more than a scant menstrual flow for a few years. He has treated eighteen or twenty patients and several who have menstruated more or less regularly.

DR. PAVLIK, in closing, said that a great deal depended upon the mentality of the individual. If the woman is fairly intelligent and one can explain to her that on account of her condition pregnancy is out of the question and that menstruation is not necessary to her well-being, she may go along without much disturbance. Unfortunately, they are not all of that type, so in cases where it is not possible to make a transplant with the blood supply of the ovary intact, Dr. Pavlik believed that cutting out as much of the healthy ovary as possible and transplanting it is an advantage to the patient even if it remains in place for only six months or a year. Most of the patients in the series were service cases from the Cook County Hospital and naturally difficult to follow-up. Some of these ovaries probably became cystic. Just because a patient does not always return, this should not lead the operator to believe he has cured the patient.

DR. J. P. GREENHILL read a paper entitled **Vaginal Discharge Due to Trichomonas Vaginalis.** (For original article see page 870.)

DISCUSSION

DR. CARL H. DAVIS said that recently he had found these organisms in two cases. These patients had been in the habit of taking douches just before coming to the office; on one occasion they both came without having taken a douche and the organisms were found.

As regards treatment, it would seem that the use of a lactic acid douche as part of the treatment might favor recurrence of the infection if it is true that these organisms can only live in an acid media. Lynch states that cultures can only be grown in acid broth. A treatment which seemed to work very nicely in one of his patients was to thoroughly dry out the vagina then to fill the vault with an alkaline powder, thoroughly rubbing it into every crevice. When she returned the next week the irritation in the vagina had practically cleared up. She had no discharge and there was no microscopic evidence of the infection.

DR. IRVING F. STEIN said that he had looked for trichomonas in cases with intractable leucorrheas, with profuse discharge, itching, burning and odor, and found them in a number of cases but was never convinced that they were the causative organisms, believing them to be contaminators. He had never used the acid treatment. He has used alkaline treatment, even resorting to the old alkaline powder, "bolus alba."

One patient who developed this type of leucorrhea two years after a vaginal hysterectomy done in another hospital, came in with a granulomatous mass in the vault of the vagina. Dr. Stein removed this with the cautery and on section it proved to be a fallopian tube which had prolapsed into the vagina. She was relieved of the discharge for a time but a year and a half later came in with this typical greenish, foul, acrid discharge in which the trichomonas were found. He treated her for some time without success.

DR. GREENHILL, in closing, said that the patients are specifically instructed not to take douches on the morning they come for treatment, because sometimes the douche removes the organisms chemically or mechanically. The organisms live in any medium, acid or alkaline.

Lactic acid is prescribed because it tends to reestablish the normal bacterial flora. A number of German and Russian obstetricians prescribe douches of lactic acid before and during labor and claim they have definitely reduced their mortality and morbidity because of this procedure. Lactic acid douches more nearly restore the normal bacterial flora than anything else. Dr. Greenhill said he also had tried alkalies some years ago but without success.

All the patients in this series were treated because they actually complained of the discharge and only those patients were included whose last treatment was given at least two months ago.

DR. ALEXANDER M. CAMPBELL read a paper on **Chorea Gravidarum**. (For original article see page 881.)

DISCUSSION

DR. CAREY CULBERTSON said that as the speaker was inclined to put this complication on an infectious basis, a review of the whole subject of chorea is in order. Chorea has not been considered in that light and he was not aware that the neurologists have placed it in that category. Dr. Culbertson said he was interested in knowing the character of the children born of choreic mothers, and asked whether in the review of the literature the cases reported disclosed the character of the children not only anatomically but mentally. Some choreics are definitely subnormal; some of the mild types are plainly enough intelligent and capable of education but some of them are not. Some of them are imbeciles.

DR. FRED H. FALLS asked if there was any evidence in the literature of a transmission of this infection to the child; if the children had any choreic spasms shortly after birth. He believed chorea was an infectious process. Rosenow recovered streptococci from the blood of choreics. Whether or not that proves to be a definite etiologic factor in the cause of chorea, time will tell. Dr. Falls cited a rare case that proved to be Huntington's chorea. The woman went through labor and delivered the baby and the baby lived. He did not feel it was necessary to induce labor. She had about the same degree of chorea when she left the service as before delivery. He had some experience with choreics at the Cook County Hospital but in none of these was a cesarean section performed. His feeling was that the danger from cesarean section with the inability to control the patient was greater than to allow her to go on and abort spontaneously in early cases or to let her deliver through the natural passages under ether when term was near.

DR. J. P. GREENHILL said that at the Chicago Lying-In Hospital he recalled two patients with chorea. One miscarried and the other went through two pregnancies and delivered spontaneously both times.

DR. ABRAHAM F. LASH said he saw one case of chorea gravidarum at the Cook County Hospital in 1922 of a woman in her fourth pregnancy and it was the first time she displayed symptoms of chorea. Dr. Lee aborted her vaginally and the chorea subsided. Two years later she returned to the hospital when four months' pregnant and again showing symptoms of chorea which rapidly became

worse. Dr. Hillis did an abdominal hysterotomy, following which the chorea subsided up to the extent that she only had slight movements in her left hand.

DR. I. F. STEIN said he was not aware that there was so high a fetal or maternal mortality in chorea gravidarum until Dr. Campbell brought it out. He recalled two cases of chorea occurring in two sisters who had been in and out of Michael Reese Hospital many times in many years. They both had chorea in adolescence and both had it in two successive pregnancies. In neither was labor induced. They were treated by rest in bed and isolation from visitors and delivered spontaneously.

He did not think medication was important, but rest in bed was a necessity. He had seen no deaths in either the mothers or babies, though their series included perhaps five or six cases.

DR. RALPH REIS said that the two sisters referred to by Dr. Stein had had five children. The smaller one of the two was a high grade moron. She had had three children. She was met in the hallway of the hospital and a diagnosis of the third pregnancy was made on sight by the fact that she had again developed a chorea. In this patient choreiform movements were only present during pregnancy.

DR. CAMPBELL, in closing, said he found nothing in the literature concerning the mentality of the children of choreic mothers. He doubted very much whether neurologists would accept infection as a sole etiologic factor, but the work of certain German investigators formed the basis for this conclusion and he felt that sooner or later the neurologists would have to accept it. However, he would not give the impression that all cases were of infectious origin. Poynton, Paine and Holmes isolated an organism, inoculated rabbits, produced choreic movements in them and recovered the organism.

Dr. Campbell was not radical on cesarean section, but felt that the operation was justifiable in the case cited. The woman was of a low type mentally and he preferred to do a cesarean section and sterilization at the same time.

The fetal mortality of fifty per cent included the abortions, miscarriages and premature deliveries. From the literature, he is convinced that the maternal mortality is exceedingly high.

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

Selected Abstracts

Endometriosis

Waeggeli, C.: Heterotopies of Uterine Mucosa. Gynécologie et Obstétrique, 1926, xiv, 158.

Endometrial transplants are most often found in the ovaries, on the pelvic and intestinal serosa, and in the rectovaginal pouch. It has been shown that they are only found in women of full sexual maturity and that they take part in all phases of the menstrual cycle. Also decidual transformations have been described. They are found occasionally on the serous surface of the uterus.

The author believes that there exists a predisposition to weakness of the uterine muscle favoring its invasion by the endometrial mucosa. In regard to Sampson's theory the author holds that there can be no doubt of a back flow from the uterus through the tubes into the abdominal cavity. Halban's theory of the formation of metastases through the lymphatic channels so far has not been confirmed by others. There are definite objections. The author thinks that various types of this growth may have various origins. Thus uterine adenomatosis is no doubt due to direct invasion. The transplants in the peritoneal cavity probably occur according to the idea of Sampson, but in certain other cases from the wolffian or müllerian tubes, etc. The author rejects for the time being the metaplasia theory and the theory of Halban.

In the majority of cases the outstanding symptom is an intractable dysmenorrhea, sometimes with metrorrhagia. Further symptoms will be due to progression and the various reactions occurring in various types of growth. The uterus is generally enlarged, often retroverted and fixed and frequently closely adherent to the rectum. A very characteristic finding is the presence of rather firm nodules in the uterosacral ligaments, pouch of Douglas, rectum, or base of the anterior culdesac. There is apt to be a primary or secondary sterility. The prognosis appears good, for in spite of their tendency to proliferate and disseminate, these growths show no malignant tendency. Malignant degeneration has only very exceptionally been observed. The treatment is surgical. X-rays have not been efficacious. Experience has shown that where complete removal of the growth is impossible, a partial extirpation will halt development. Ovarian castration brings about an atrophy of the growths which are under the domination of the ovarian secretion. The author wonders if certain peritoneal and retroperitoneal cysts originating in embryonic inclusions may not be the beginnings of these growths. He even suggests that pseudomucinous cysts of the ovary might start from uterine mucosa transplanted on the surface of the ovary.

GOODRICH C. SCHAUFFLER.

Halban, J.: Hystero-adenosis Metastatica. The Lymphatic Origin of the So-Called Adenofibromatosis Heterotopica. Archiv für Gynäkologie, 1925, cxxiv, 457.

Halban reports five cases of this condition which he prefers to call hystero-adenosis metastatica rather than heterotopic adenofibromatosis, adenomyosis, endometrioma,

chocolate cysts, etc., as other investigators have named tumors containing uterine mucosa and found in the pelvic and abdominal organs other than the uterus. He believes that these tumors are true metastases carried from the uterus by way of the lymphatics and shows that they are always found along the course which the uterine lymphatics follow in the abdomen. He feels, however, that these metastases are benign.

Halban disagrees with the implantation theory of Sampson because he cannot believe that uterine mucosa, which during menstruation is necrotic, dead and stains poorly, can be active enough and alive enough to grow again if it comes in contact with other structures. Secondly, he cannot understand how such a mucosa could penetrate the thick tunica albuginea of the ovary. He also states that it is impossible to reconcile the implantation theory with these structures when found in the umbilicus and in laparotomy scars.

The lymphatic distribution of such bits of uterine mucosa which, when deposited on various structures, develop hyperplastically is proved by the following facts: Meyer, Frankl, Lahn and others have demonstrated the existence of bits of uterine mucosa in the lymphatics of the uterine wall and have traced them to the serosa of the uterus. There then seems to be no reason why the lymphatics cannot carry such bits of endometrium along their entire course and deposit them at various points throughout the abdomen. Secondly, Ries, Wertheim and others have found bits of uterine mucosa in all the regional lymph glands, i.e., inguinal, sacral, iliac and parametrial groups of glands. Thirdly, these masses of epithelial cells resembling uterine mucosa are never found in the male but only in the female, and only, in the female, in those glands which receive the lymphatics from the uterine wall.

Since the lymphatics from the uterus drain into the rectovaginal septum, toward the ovary, mesosigmoid and mesoappendix, umbilicus and abdominal wall, all growths in these locations and even in laporatomy scars, can readily be explained by the theory of lymphatic distribution.

RALPH A. REIS.

O'Keefe, C. D., and Crossen, R. J.: Autotransplantation of Endometrial Tissue in Dogs. The Journal of the Missouri State Medical Association, 1927, xxiv, 252.

The authors experimented on ten dogs. They obtained transplants in only two cases but believe that the failures were due to technical shortcomings and had nothing to do with the tissue vitality. They believe that the outcome of their experiments tends to support Sampson's theory.

A. C. WILLIAMSON.

Spirito, Frencesco: Genesis of Endometriomata. Archivio di osteticia e ginecologia, 1927, xiv, i.

Spirito transplanted pieces of uterine mucosa, pieces of the uterine wall, peritoneal scrapings, pieces of the peritoneum, ovarian epithelium, small pieces of ovary, intestinal mucosa, stomach and esophagus and found that the only tissue which would grow upon the peritoneum was uterine mucosa. This growth showed all the histologic characteristics of uterine mucosa with cystic glands.

He also made a uteroabdominal fistula and injected air into the uterus and through the tubes into the abdominal cavity. At autopsy all these animals showed cystic growths on the peritoneum of either the pelvis or the abdominal cavity, or both.

He believes that his researches help to substantiate Sampson's theory as to the

origin of endometriomas. He says, however, that he cannot satisfactorily explain why the Rubin insufflation procedure does not also produce endometriomas.

J. M. PIERCE.

Jacobson, Victor C.: Intraperitoneal Transplantation of Endometrial Tissue. Archives of Pathology and Laboratory Medicine, 1926, i, 169.

The author experimentally transplanted endometrial tissue in rabbits and monkeys (macacus rhesus). Only autotransplants were used. Of the 19 rabbits experimented on during estrus, the grafts were successful in 16 cases. In 6 operated upon during pregnancy, implantation was successful in 2. The ectopic growths which were invariably cystic adenomas were recovered from the pelvic viscera and in some cases from the large bowel, on its peritoneal surface.

Of the 5 monkeys so treated the curetted transplants were more confined to the uterus and adhesions about it. The "reaction to implantation" was studied at three weeks, eight months, and one year after the operation. In one case the ectopic endometrium was found in the menstrual stage. The successful autotransplantation of endometrium in both experimental animals used in this series is analogous to the phenomenon of ectopic endometriosis in the human female with respect to location, histology and response to ovarian secretion. This experimental work further substantiates Sampson's theory of the origin of ectopic endometriosis in the human.

W. B. SERBIN.

Lemon and Mahle: Ectopic Adenomyoma: Postoperative Invasion of the Abdominal Wall. Archives of Surgery, 1925, x, 150.

Lemon and Mahle observed nine patients with adenomyoma occurring in the scar of an abdominal operation. In none of these cases were adenomyomas demonstrable in any other location. All of the patients has been subjected to operations on the female genitalia at some previous time. Histologically all of the tumors examined presented the usual picture of adenomyoma with connective tissue and smooth muscle stroma and typical endometrial tissue and occasional cysts filled with blood and cell débris.

The authors review the various theories advanced as to the origin of ectopic adenomyoma quoting all the more or less obsolete ideas on the subject but, strangely enough, ignore absolutely the extensive work on this subject by Sampson. On the other hand they advance as a plausible theory of their own that they may be due to uterine mucosa transplanted at the time of operation.

R. E. WOBUS.

Maes, Urban: Endometrioma of the Abdominal Wall: American Journal of Surgery, 1927, xi, 539.

Maes endeavors to throw further light on the etiology of endometrial cysts in the publication of his article dealing with a tumor in a scar of the abdominal wall. He reopens the argument fostered by Novak and Sampson and rather agrees with Novak. However, he is inclined to agree with Judd in the explanation of his own case in that the transplantation is brought about by means of the needle and suture materials passing through the endometrium and bringing fragments of it to rest in the abdominal musculature. Mae's patient, eight years previously, had had a supravaginal amputation and soon afterward the abdominal scar began to hypertrophy. Small cystic cavities formed from which sanguinous fluid was evacuated. The scar was removed and microscopically showed endometrial transplants.

WILLIAM KERWIN.

Kitai, I.: The Inflammatory Origin of Atresia and of Heterotopic Epithelial Proliferation in the Tubes. Archiv für Gynäkologie, 1926, cxxviii, 413.

On the basis of careful microscopic studies made on seven cases, Kitai concludes that atresia and heterotopic proliferation of the mucosa almost always follow inflammation of the tube and are not due to congenital malformations. These latter have been demonstrated in almost every portion of the female genital tract but have never been found in the tubes. The hypothesis of malformations, as advanced by Schidde and Schoenholz, cannot explain the excessive growth and heterotopic proliferations which are occasionally found in the tubes. Every instance of such atresia with heterotopic proliferation can easily be explained on the basis of a preexisting inflammation with the resulting inflammatory changes. These are usually gonorrheal in origin.

RALPH A. REIS.

Cordua, R.: Epithelial Hematomata and Endometroid Formations of the Ovary. Archiv für Gynäkologie, 1926, cxxviii, 617.

Cordua concludes that epithelialized hematomas of the ovary may originate from various sources such as corpus luteum hematomas or interstitial hemorrhages which become lined with epithelium by an ingrowth from the germinal layer, or from endometroid formations or other types of epithelialized cysts. Such hematomas are produced by the tendency to bleed which exists at the menstrual periods and they apparently bleed repeatedly.

The author leans toward the theory of endometroid formation from serosa epithelium and does not feel that the implantation theory has been satisfactorily proved.

RALPH A. REIS.

Dawson: Ovarian Pregnancy and Endometrioma. Medical Journal of Australia, 1926, ii, 233.

The writer believes that the comparatively frequent occurrence of ectopic endometrial tissue in the vicinity of the ovaries has an important influence on the origin of the ovarian pregnancy. Spermatozoa not uncommonly reach the pelvic cavity. Graafiian follicles are maturing and ova being liberated and nevertheless ovarian pregnancy but rarely occurs. The reason for this rarity, he believes, is that another factor is required: namely, the presence of some endometrial tissue. Transplanted endometrial tissue in or about the ovary provides what may be called a miniature auxiliary womb. The writer has collected considerable suggestive evidence in favor of his viewpoint; thus he states that the possibility of fertilization of the ovum within the pelvic cavity is generally accepted. Secondly, consideration of the philogenetic attraction between zygote and endometrial mucosa suggests that the latter is an essential factor in the implantation of the impregnated ovum. Thirdly, the comparative frequency of impregnation taking place in the pelvis and the extreme rarity of ovarian pregnancy suggests the necessity of another factor for its occurrence. Fourthly, in many carefully examined and described specimens of ovarian pregnancy it is clear that impregnation did not occur in the graafian follicle for a maturing corpus luteum can be seen separate and distinct from the gestation sac. Finally, the coexistence of endometriomas of other pelvic viscera and ovarian pregnancy has been seen in at least one case.

The writer reviews cases which tend to further bear out his views.

NORMAN F. MILLER.

Books Received

DIATHERMY. By Elkin P. Cumberbatch, medical officer in charge, electrical department, St. Bartholomew's Hospital, etc. Second edition. C. V. Mosby Co., St. Louis, 1928.

RECENT ADVANCES IN CHEMISTRY IN RELATION TO MEDICAL PRACTICE. By McKim Marriott, B.S., M.D., dean, and professor of pediatries, Washington University School of Medicine, etc. Illustrated. C. V. Mosby Co., St. Louis, 1928.

TROPICAL GYNAECOLOGY. By V. B. Green-Armytage, professor of obstetries and gynaecology, Medical College, Calcutta, etc. Calcutta and Simla, Thacker, Spink and Co., 1928.

THE TECHNIC OF LOCAL ANESTHESIA. By Arthur E. Hertzler, professor of surgery in the University of Kansas, etc. Fourth edition. With 146 illustrations. C. V. Mosby Company, St. Louis, 1928.

BLOOD AND URINE CHEMISTRY. By R. B. H. Gradwohl, director of the Gradwohl laboratoratories, and Ida E. Gradwohl, instructor. With 117 illustrations and 4 color plates. C. V. Mosby Co., St. Louis, 1928.

GREFFE OVARIENNE ET ACTION ENDOCRINE DE L'OVAIRE. Par Vittorio Pettinari. Avec 181 figures dans le texte. Paris, Gaston Doin & Cie, 1928.

Erratum

In the discussion of Dr. B. P. Watson's paper entitled "An Outbreak of Puerperal Sepsis in New York City," which was read at a meeting of the New York Obstetrical Society of which the transactions were published in the August issue of this Journal, the remarks made by Dr. J. Milton Mabbott were unfortunately omitted from the record and are herewith presented in substance.

Discussing this subject Dr. Mabbott said that he desired to refer particularly to the treatment of puerperal sepsis and stated his belief that the results as regards the mortality from this complication of pregnancy were as good forty years ago as they are today. He felt that at least a small proportion of the cases in an epidemic of puerperal sepsis should be subjected to a trial treatment by the vaginal douche early and the intrauterine douche later on in the course of the disease in patients in whom the streptococcus is found in the vagina and in whom it is assumed that probably a good deal of the infection goes through the lymphatics from the cervix and uterine cavity.

Dr. Mabbott then referred to the use, at a later period, of vaccines in puerperal sepsis and instanced a case in his private practice of a remarkably favorable response within twenty-four hours after a single subcutaneous injection of a stock culture. In view of this experience Dr. Mabbott would reply to Dr. Meleney's question as to what should be done in a case of puerperal sepsis by saying "use a vaccine."

Finally the experience in the late war, with infected wounds, should teach us the wisdom of protecting the vagina and uterus against infection by doing away with the contained lochia. In the presence of the streptococcus hemolyticus, such lochial discharges would serve as an excellent culture medium and should therefore be cleaned out by the means already referred to.

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BROOKLYN GYNECOLOGICAL SOCIETY; ST. LOUIS GYNECOLOGICAL SOCIETY;
NEW ORLEANS GYNECOLOGICAL AND OBSTETRICAL SOCIETY
CHICAGO GYNECOLOGICAL SOCIETY

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Mead's Standardized Cod Liver Oil

is accepted as a criterion of excellence by physicians and by other pharmaceutical houses. *It is an established measure of quality regulated by a standard.*

A more definite description will be found on back cover and on inside back cover page.

MEAD JOHNSON AND COMPANY, Evansville, Indiana, U. S. A.
Manufacturers of Infant Diet Materials Exclusively

Less Than a Minute to Read This —a Minute Well Spent

What is SISTOMENSIN, "CIBA"?

SISTOMENSIN, "CIBA" is the ovarian hormone obtained by a special patented process.

Where is SISTOMENSIN, "CIBA" indicated?

SISTOMENSIN, "CIBA" is indicated in functional menorrhagia, in functional dysmenorrhea, in sterility due to hypoplasia, and in amenorrhea when due to hypoplasia. To relieve the nervous disorders of artificial and natural menopause.

Is SISTOMENSIN, "CIBA" standardized?

Yes—by both the Allen-Doisy and the Herrman tests.

How is SISTOMENSIN, "CIBA" issued?

Tablets 1/5 gr. each—bottles of 40 tablets.
Ampules 1 c.c. (4/5 gr.)—cartons of 5 and 20 ampules each.

Is SISTOMENSIN, "CIBA" easily available?

Yes. At your druggists. SISTOMENSIN, "CIBA" is obtainable through any drug jobber.

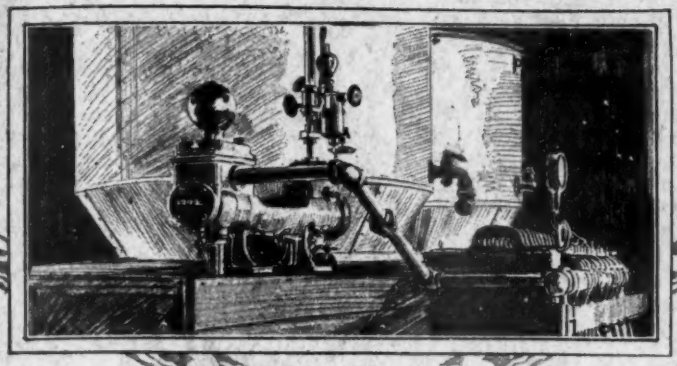
Samples and literature will be gladly sent you upon request.

CIBA

PURITY RELIABILITY EFFECTIVENESS

CIBA COMPANY, Inc.

Cedar & Washington Streets **New York City**



Steam Rendering Vats

Steam Rendering of Cod Livers

Vs Rotting

Much of the unpleasantness in the taste of cod liver oil was eliminated when steam was introduced to remove the oil from fresh livers.

The old method, when the industry was in its infancy, was to allow the livers to rot in open barrels in the sun. Putrefaction and nature were relied upon under the old order. Science and progress mark the new

This added to the fact that only about an hour's time elapses from the time the fish are caught until the livers are in the rendering vats, accounts in large measure for the superiority of Mead's Standardized Cod Liver Oil.

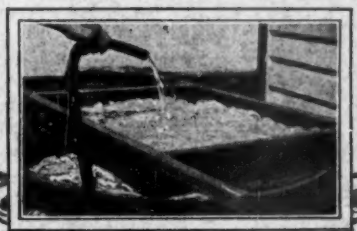
But before rendering, each liver is examined and thoroughly washed. Bile infected and small livers are thrown out. These are all preparatory precautions.

And now Mead's Cod Liver Oil can be had with the addition of agreeable essential oils—permanently flavored—with no diminishing of potency or injury to the patient.

MEAD JOHNSON & COMPANY

Evansville, Indiana

Above Center: Rotting Livers Old Method



At Left: Washing Livers Before Rendering

Samples and Literature on Request

NO!

The P.C.A. and P.H A. have not removed from Omaha, Nebraska

At the same location for nearly 27 years, paying more money for claims and using less for expenses than any concern offering sickness and accident insurance to Physicians, Surgeons and Dentists.

Assets—$800,000.00.—Assures ability to pay.

Elimination of profits insures inclination to pay all just claims promptly.

State deposit of $200,000.00 for protection of all members.

Total claims paid exceed $3,500,000.00.

PHYSICIANS CASUALTY ASSOCIATION
PHYSICIANS HEALTH ASSOCIATION
E. E. ELLIOTT, Secretary
304 City National Bank Building Omaha, Nebraska

Taste of Cod Liver Oil

Mead's Flavored Cod Liver Oil is especially indicated for runabouts and older children who have an aversion to the taste of plain cod liver oil. The delicate flavor resembles honey, and there is no after-taste or repeat after swallowing. Only 12 drops of flavoring are added to each pint of *biologically tested* oil made in our own rendering stations in Newfoundland.

Samples and literature furnished cheerfully on request.

☐ For Private Practice
☐ For Clinic

MEAD JOHNSON & COMPANY
EVANSVILLE, INDIANA, U. S. A.

MANUFACTURERS OF INFANT DIET MATERIALS EXCLUSIVELY